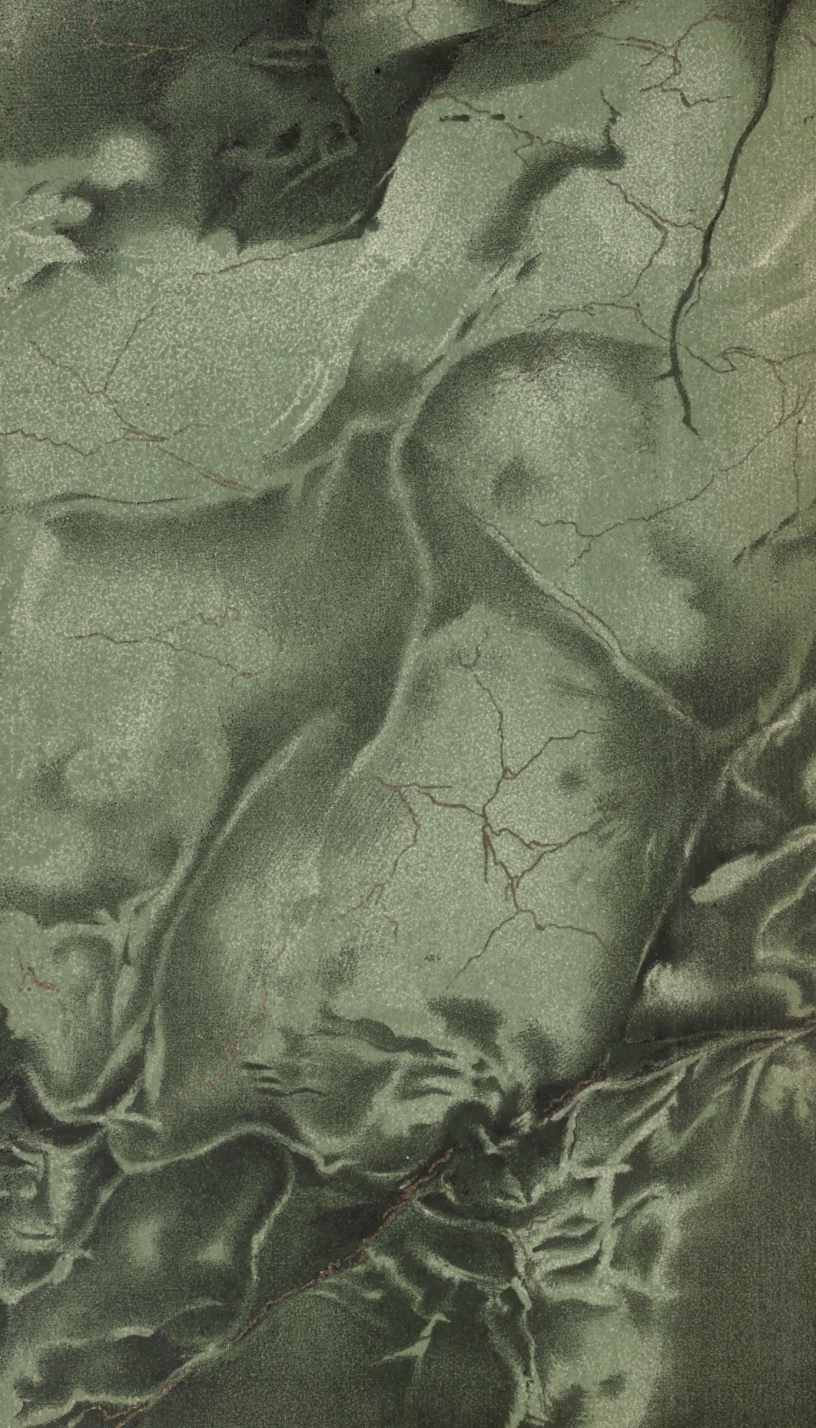

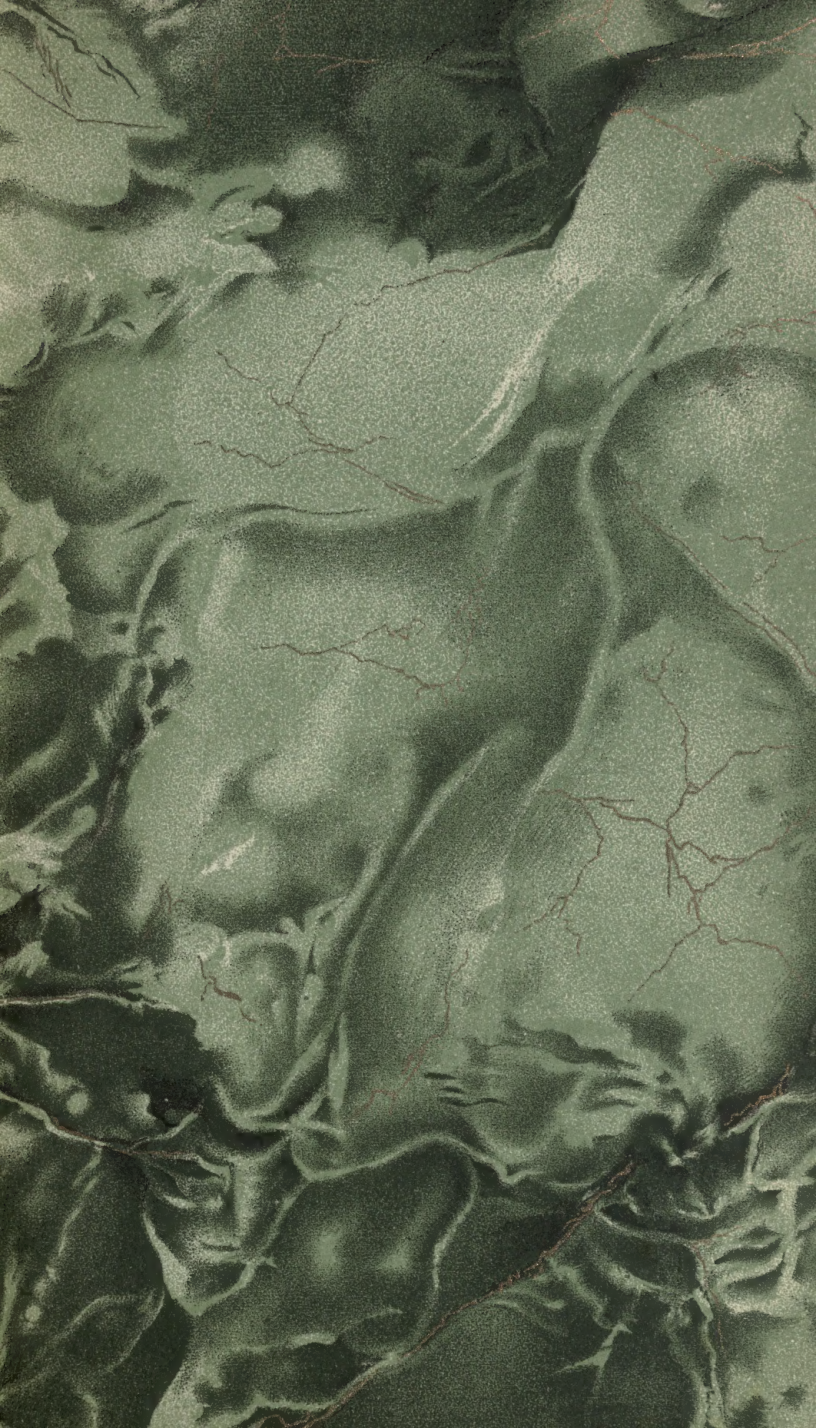

ANNUAL REPRINT OF THE REPORTS

OF THE

COUNCIL ON PHARMACY AND CHEMISTRY

OF THE

AMERICAN MEDICAL ASSOCIATION

FOR 1915

WITH THE

COMMENTS THAT HAVE APPEARED
IN THE JOURNAL

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PREFACE

The reports of the Council on Pharmacy and Chemistry of the American Medical Association have appeared from time to time in THE JOURNAL. The more strictly scientific parts of the reports, however, both from lack of space and because of their technical nature, have been abstracted or entirely omitted from the reports thus published. Believing that these scientific investigations should be available to scientists in general, especially to chemists, pharmacologists and others interested in medicine, the Council has authorized the preparation of this volume, containing the complete reports of the council adopted prior to Jan. 1, 1916, as well as the comments which have appeared at the time of publication.

In previous years by far the greater portion of the Council's investigations have not been published for two reasons. First, it was thought that many of the products found ineligible did not justify reports because they were of interest to few physicians; and, second, it was desirable that the manufacturers should be given an opportunity to modify or improve the preparations found ineligible and thus make them acceptable to inclusion in N. N. R.; therefore, publication of reports dealing with rejected articles was postponed so far as possible. The Council having been in existence for nearly ten years, manufacturers have had ample time to adapt themselves to new conditions, and one of the reasons for delayed publicity no longer holds good. So far as the other reason is concerned, inquiries which come to the Council and to THE JOURNAL indicate that physicians do, for various reasons, seek information in regard to many proprietary products regarding which no report has been published. The Council, therefore, has decided to make public, even when no detailed reports are prepared, a brief outline of the reasons which led to the rejection of articles, and has authorized the publication of the abstracts which appear at the end of the present volume, under the heading "Abstracts of Council Action."

CONTENTS

PAGE

Tri-Iodides, Three Chlorides and Maizo-Lithium..... 9
Sanmetto 17
Neurilla 20
Peacock's Bromides and Chionia..... 24
Chemotherapy and Tumors..... 28
Secretogen 46
Burnham's Soluble Iodine..... 50
Venarsen 52
Gray's Glycerine Tonic..... 56
Tongaline and Ponca Compound..... 58
Alfatone 62
Formamint 64
Iodum-Miller and Iod-Izd-Oil (Miller's)..... 76
Lactopeptine and Elixir Lactopeptine..... 79
Proprietary Digitalis Preparations..... 89
Protonuclein and Protonuclein Beta..... 90
Digitalysatum 93
Hydropsin 94
So-Called Secretin Preparations..... 96
Has Secretin a Therapeutic Value?..... 99
Delays in Passing on Products..... 119
Intravenin P-H 120
Lecithin Preparations Omitted from N. N. R..... 122
Pantopon Roche (Pantopium Hydrochloricum) Accepted for N. N. R..... 126
Proprietary Names for Liquid Petrolatum..... 127
Radelium and Radelium Generator..... 128
Seng 129
Abstracts of Council Action..... 131
G. G. Phenoleum Disinfectant..... 131
Phytin and Fortossan..... 131
Virol 132
Salesthyl and Sal-Hyl..... 134
Analutos and Analutos Tablets..... 135

PAGE
Budwell's Emulsion of Cod-Liver Oil, Nos. 1 and 2... 135
Colchi-Sal 136
Waterbury's Compound 138
Hagee's Cordial of the Extract of Cod Liver Oil Compound 138
Wampole's Perfected and Tasteless Preparation of an Extract of Cod Liver..... 140
Veracolate 141
Taurocol 143
Lactobacilline, Omitted from N. N. R..... 143
Iodex 144
Venodine 145
Calcreose 147
Standard Radium Solution for Intravenous Use..... 147
Rheumalgine 148
Uricsol 149
Duodenin, Armour 151
Jubol 152
Urodonal 153
Hydragogin 154
Williams' Syrup of Malt..... 155
Filudine 156
Globeol 157
Hexa-Co-Sal-In 159
Swan's Rheumatic Bacterin (Mixed) No. 47..... 160
Elixir Iodo-Bromide of Calcium Comp. "Without Mercury" and "With Mercury"..... 160
Agurin Tablets, Alypin Tablets, 3½, 1⅛ and ⅓ grain, Hedonal Tablets 8 grains, Iodothyrine Tablets 5 grains, Tannigen Tablets, Cocaine and Adrenalin Ointment-M. E. S. Co., Dolomol Pyrogallic Acid 5 per cent., Dolomol Chrysarobin 5 per cent., Dolomol Europhen 10 per cent., Dolomol Naphthol 5 per cent., Dolomol Salol 10 per cent., Dolomol Tar 10 per cent., Dolomol Thymol 2 per cent., and Xerase Capsules, Omitted from N. N. R..... 162
Anistamina 162
Antipyrin Salicylate-Farbwerke, Betanaphthol Benzoate-Heyden, Betol-Heyden, Bornyval, Euphorin, Eupyrine, Fortoin, Quinine Lygosinate, Sodium Lygosinate, Friedländer Bacterin-Mulford, Predigested Liquid Food-Mulford, Guaiacodeine and Gujasanol, Omitted from N. N. R..... 164

PAGE
Frosst's Blaud Capsules 164
Brobor (Episan) 164
Bromo-Mangan, Omitted from N. N. R. 165
Elixir Buchu, Juniper and Acetate Potassium, Omitted from N. N. R. 166
Tyree's Elixir of Buchu and Hyoscyamus Compound .. 167
Syrup Cannabis Compound, Omitted from N. N. R. .. 168
Calol Liquid Petrolatum, Omitted from N. N. R. 168
Chinaphenin, Omitted from N. R. R. 168
Colchi-Methyl Capsules, Omitted from N. N. R. 169
Emulsio Minerolein and Emulsio Phen-Oleum 169
Glutol-Schleich, Omitted from N. N. R. 170
Pill Glycero-Lecithin 170
Hydroleine 171
Isatophan and Paratophan, Omitted from N. N. R. 172
Koyol 172
Med-O-Lin 172
Methyl-Santal, Omitted from N. N. R. 173
Neurocaine, Omitted from N. N. R. 173
Oxyntin, Omitted from N. N. R. 174
Piperazine-Schering, Omitted from N. N. R. 174
Ricinol-Grape Tape-Worm Remedy and Baby Taenia-fuge-Grape 174
Tubo-Arg 175
Ulax Salt 175
Uranoblen and Caviblen 176
Curative Vaccine, Bruschettini 177
Stearns' Wine 177

Reports of the Council on Pharmacy and Chemistry

TRI-IODIDES, THREE CHLORIDES AND MAIZO-LITHIUM

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., Feb. 6, 1915, p. 528*)

As an illustration of the unreliability of claims and unscientific character of proprietary mixtures, the Council has authorized publication of the following reports on Tri-Iodides, Three Chlorides and Maizo-Lithium, products of the Henry Pharmacal Co. (J. F. Ballard, proprietor).

W. A. PUCKNER, Secretary.

Tri-Iodides (Henry)

Tri-Iodides (Henry Pharmacal Co., St. Louis) is a nostrum whose ingredients apparently were selected at random. Since the effects of such a mixture cannot be predicted, no thoughtful physician would think of prescribing in any one condition all the drugs named in the formula of Tri-Iodides—if he had to write out the prescription. Yet because the misleading name of the preparation gives it the semblance of a therapeutic entity—and because it is advertised in medical journals—a certain number of physicians thoughtlessly prescribe this shotgun mixture.

LABORATORY REPORT

Regarding the composition of "Tri-Iodides" the Association's Chemical Laboratory makes the following report:

A trade package of Henry's Tri-Iodides purchased in 1910 bore the following formula on the label:

"Colchicin, 1-20 grain,
"Phytolaccin, 1-10 grain,
"Solanin, 1-3 grain,
"Sodium Salicylate, C. P., 10 grains,
"Iodic Acid (equal to 7/32 gr. of Iodine) in two fluid drachms of Aromatic Cordial."

In the circular which was wrapped with the bottle the wording of the formula differs somewhat from the foregoing, "iodic acid" of the label being replaced by "hydro-iodic acid." While the label on the bottle named

"phytolaccin" as one of the constituents the label on the carton which contained the bottle gave "decandrin." The following formula appears on a trade package purchased June, 1914:

"Colchicine, 1-200 Grain,
"Phytolacca, 1 1-5 Grain,
"Mydriatic Alkaloids, 1-500 Grain.
"Sodium Salicylate, 3 1-2 Grain.
"Iodic Acid (equal to 7-125 Grain of Iodine) in two fluid drachms."

The differences between the formulas are striking. Colchicin has been reduced from $\frac{1}{20}$ grain to $\frac{1}{200}$ grain; sodium salicylate from 10 grains to $3\frac{1}{2}$ grains; iodin (claimed to be present as iodic acid) from $\frac{7}{32}$ grain to $\frac{7}{125}$ grain. "Phytolaccin" ("Decandrin") has been replaced by "Phytolacca" and "Solanin" by "Mydriatic Alkaloids." While the formula for the preparation has been changed, the circular accompanying the package still refers to "solanin" (in some parts of the circular wrongly spelled "salonin") and "phytolaccin." As no principle having the characteristic effects of poke-root is known to have been isolated the terms "decandrin" and "phytolaccin" are meaningless.

The circular states that solanin is an alkaloid obtained from the sprouts of *Solanum tuberosum,* but wrongly calls this plant "bittersweet" instead of potato. At the market price the amount of solanin claimed, according to the old formula, to be present in a bottle of Tri-Iodides, would cost $1.60, although a bottle of the preparation sold at wholesale for 67 cents.

Tri-Iodides is a dark brown, mobile liquid having a faint clove-like odor and a mawkish, sweet taste. Salicylate was found in considerable amounts. Traces of alkaloids were found, a portion of which appeared to be colchicin. Iodic acid and its salts were absent, although claimed by the formula to be present. Potassium iodid was present. Determinations of the iodin by distillation with ferric ammonium sulphate solution and sulphuric acid indicated the presence of about 1.68 gm. of iodin (equivalent to 2.18 gm. of potassium iodid) in each 100 c.c. of the preparation. This is equivalent to about 7.65 grains of iodin per fluidounce, or more than thirty-four times the amount claimed by the formula on the bottle. An approximate determination of the salicylic acid by extraction of the acidified preparation with ether and evaporation of the solvent indicated about 2.67 gm. in 100 c.c., equivalent to 3.09 gm. of sodium salicylate, or about 14.11 grains per fluidounce. Since the amount of sodium salicylate claimed is 3.5 grains in 2 fluidrams or 14 grains in each fluidounce, the amount found agrees essentially with the claims.

ABSURD CLAIMS

It should be unnecessary, after pointing out the conflict between the name and the published formula, between the formula and the actual composition, and between the composition and all established therapy, to discuss this heterogeneous and unscientific mixture further. A few specimen absurdities, however, may be quoted from the advertising "literature":

". . . Free of the Disagreeable Effects of the Alkaline Iodides."

[Tri-Iodides, according to the laboratory report, depends for its iodin action on potassium iodid.]

". . . we have an assimilable form of vegetable hydriodates. "The hydriodates of these valuable vegetable alkaloids afford the specific alterative action of iodine without such disagreeable results as the iodism produced by the ordinary iodides."

["The hydriodates" is an obsolete term formerly applied to iodids of vegetable alkaloids. Iodids of vegetable alkaloids, if present at all in Tri-Iodides, are present in negligible amounts.]

"Containing Iodine in an available form, it is obvious that the formula must be beneficial in the majority of syphilitic skin lesions."

The falsity of the first two of these claims and the mischievousness of the last are self-evident.

It would be possible, but is unnecessary, to produce an almost unlimited amount of evidence to show the transparent character of the deception by which this preparation is exploited.

The referee feels that the nostrum will have been sufficiently characterized when he has mentioned further that the name "Henry's Tri-Iodides" is blown in the glass of the bottle, that the label contains the recommendation "For Gout, Rheumatism and other Diathetic Diseases," and that the circular accompanying the bottle recommends the use not only of Tri-Iodides, but also of Three Chlorides, Maizo-Lithium, Campho-Phenique and Satyria in the treatment of many diseases.

RECOMMENDATION

It is recommended that Henry's Tri-Iodides be held in conflict with the rules of the Council because its composition is incorrectly stated (Rule 1); because it is advertised indirectly to the public (Rule 4); because its advertising contains therapeutic exaggerations (Rule 6); because the name does not indicate the potent ingredients (Rule 8), and because the mixture is unscientific (Rule 10).

Three Chlorides (Henry)

Three Chlorides (Henry) is advertised as:

"An oxygen-carrying ferruginous preparation, suitable for prolonged treatment of children, adults and the aged. Indicated in anemia and convalescence from acute diseases and surgical operations."

The following report on the composition of Three Chlorides is submitted by the Association's Chemical Laboratory:

LABORATORY REPORT

It is claimed that each fluidram of Henry's Three Chlorides contains:

"Mercuric Bichlorid ..... 1-72 Gr.
"Arsenic Chloride ..... 1-40 Gr.
"Proto-Chloride Iron ..... 2-25 Gr.
". . . in a cordial of Calisaya Alkaloids."

The preparation is a pale yellow, clear solution having an odor of alcohol. The addition of potassium ferricyanid solution does not produce any blue coloration, thus demonstrating the absence of ferrous chlorid (iron protochlorid). Instead potassium ferrocyanid solution produces at once an intense blue precipitate and potassium sulphocyanate solution an intense red coloration, thus proving the presence of iron in the ferric condition. It is obvious that the claimed superiority of Three Chlorides over preparations containing ferric iron is absurd. Since it contains iron in the ferric condition, Three Chlorides decomposes soluble iodids with the liberation of free iodin. The assertion that it is a suitable "vehicle" for the administration of iodids is likely to lead the physician unwittingly to administer free iodin.

As the laboratory report shows, the "formula" of Three Chlorides (Henry) is incorrect, for protochlorid of iron (ferrous chlorid) was absent from the preparation. There is, however, a more serious objection to the formula than the misstatement of fact. When the physician is dealing with conditions that call for mercury, arsenic or iron, it is irrational and unscientific to prescribe a preparation containing these three drugs in fixed proportions.

OBJECTIONABLE ADVERTISING

Three Chlorides is marketed in bottles having the name "Three Chlorides" blown in the glass, in a carton containing a circular extolling the curative powers of this and other proprietaries of the same concern. Thus a physician who prescribes Three Chlorides is likely to place in the hands of his patient the advice that

"Three Chlorides . . . is suitable for the prolonged treatment of children . . ."

"In tertiary syphilis, with or without potassium iodide, it holds first rank among remedies directed against the specific taint . . ."

Further, that "Maizo-Lithium" is:

"A Genito-Urinary Sedative" and a "remarkable uric-acid solvent."

Also that "Satyria" is:

"An Ideal Genito Tonic and Nerve Reconstituent."

"Indicated in Prostatic trouble, Cystitis, Urethritis, Gonorrhea, Gleet, Leucorrhea, Sexual Debility and Impotence."

We are told that

"As a hematinic, the protochloride of iron justifies the confidence of the medical profession."

"The protochloride, more than any other salt of iron, stimulates the paptic [*sic*] and hydrochloric glandular system of the stomach, increasing the flow of acid gastric juice."

It is unnecessary to discuss the truth or falsity of these assertions, since Three Chlorides does not contain the protochlorid of iron. For the same reason, it is obvious that the small amount of iron which it contains is the only possible justification for the claim that the preparation is

". . . Non-Productive of . . . Constipation or Teeth Discoloration."

It is hardly necessary to point out that it is a therapeutic exaggeration to claim that Three Chlorides is of particular value in the treatment of tertiary syphilis, that in eczema it is "the most effective remedy," that in any form of constipation it is "the remedy par excellence," or that

"After arresting malarial attacks with quinine, the combination of iron, arsenic and mercury with calisaya is an essential requisite."

"Whenever gastric troubles and digestive disturbances furnish a contra-indication to iron, this contra-indication disappears when the iron is combined with arsenic."

"The simultaneous exhibition of small doses of arsenic and bichloride of mercury, besides augmenting the effect of iron upon the red blood-cells, completely obviates the tendency to vascular congestion and hemorrhage."

Finally, the suggestion that by the use of Three Chlorides iodids may be prevented from causing iodism is absurd.

In short, whatever may be the advisability of prescribing iron, arsenic or mercury in any given case, it is irrational to prescribe them in fixed proportions. A physician who is induced by the exaggerated advertising claims to prescribe these drugs in a proprietary mixture, under a non-informative name, does grave injustice to his patients.

RECOMMENDATION

It is recommended that Three Chlorides (Henry) be held in conflict with Rule 1 in that it does not contain protochlorid of iron (ferrous chlorid) as claimed (as shown by examination) but contains the iron in the ferric condition; for conflict with Rule 4 in that it is advertised indirectly to the public for the treatment of diseases with the likelihood of doing harm; with Rule 6, in that exaggerated and unwarranted therapeutic claims are made for the preparation; with Rule 8, in that the name of this pharmaceutical mixture does not indicate the presence of its potent constituents: iron, mercury and arsenic; with Rule 10, in that the routine administration of mercury and arsenic in combination with iron, in fixed proportions, is unscientific and a detriment to the profession and the public.

Maizo-Lithium

Maizo-Lithium (Henry Pharmacal Co., St. Louis) is one of the many proprietary lithium preparations based on the disproved theory that lithium dissolves uric acid deposits in the body. The label on a trade package states that:

"Maizo-Lithium promptly facilitates the elimination of the uric and phosphatic deposits from the system."

As might be expected, the promoter of Maizo-Lithium ascribes a long list of ills to "uric and phosphatic deposits," and argues that, therefore, Maizo-Lithium is the proper treatment:

"In lithemia, hematuria, incipient diabetes, cystitis, urethritis, pyelitis and ALL inflamed conditions requiring a non-irritating diuretic."

"Inflamed conditions," naturally, include almost all of the real or imaginary ills of kidney, bladder, etc.

Maizo-Lithium is distinguished from its congeners chiefly by the claim that it contains a mythical or problematical compound, maizenate of lithium.

LABORATORY REPORT

The following report on the composition of Maizo-Lithium has been submitted by the Chemical Laboratory of the American Medical Association:

The promoter of Maizo-Lithium makes the following statement on the label concerning the composition of the preparation:

"Each fluid drachm contains two grains maizenate of lithium."

The following is also found in a circular which is enclosed with the trade package of Maizo-Lithium:

> "Maizo-Lithium, the remarkable uric acid solvent, is a nascent chemic union of maizenic acid, obtained from green corn silk, with the alkaline base lithium forming maizenate lithium, of which the mother liquid carries two grains to each drachm."

Standard works on organic chemistry and pharmacology, such as Beilstein's Organische Chemie and Cushny's Pharmacology and Therapeutics, do not mention maizenic acid. Neither is it mentioned in compresensive bibliographies of phyto-chemical investigations, such as Huseman-Hilger's Die Pflanzenstoffe or Wehmer's Die Pflanzenstoffe. The first to use the term appears to have been a Dr. Vautier (*Arch. méd. belg.*), but his publication is not available to the laboratory. Rademacher and Fischer (*Amer. Jour. Pharm.*, 1886, lviii, 369) claim to have isolated the substance from green corn-silk, but the record of their work is unsatisfactory and indefinite and therefore their results could not be verified; it seems unlikely, however, that they isolated a pure proximate principle.

Examination of Maizo-Lithium demonstrated the absence of bromids, chlorids, phosphates, sulphates, acetates, benzoates, salicylates and tartrates—combinations in which lithium might be expected to be present. The presence of a citrate, however, was shown by the usual tests. Lithium and sodium were present. Free acid was absent. Determination of lithium citrate and of sodium citrate indicated the presence of a total of about 3.7 gm. of these two salts in each 100 c.c. of the preparation, or about 2.1 grains in each fluidram. About 25 per cent. of the total salts appeared to be lithium citrate. The examination, therefore, does not demonstrate the presence of "maizenate of lithium," but does show that Maizo-Lithium contains a mixture of lithium citrate and sodium citrate. Tests for citric acid and citrates were made on a commercial specimen of fluidextract of corn-silk. The results were negative, although the preparation had an acid reaction to litmus. The presence of maizenate of lithium in Maizo-Lithium—in fact, its actual existence—thus failed of demonstration. In view of this fact, it was felt that the burden of proof rested on the promoter of Maizo-Lithium to supply some satisfactory evidence with regard to this substance. The following letter was, therefore, sent to James F. Ballard:

> "According to the label on a recently purchased bottle of Maizo-Lithium, each fluidram of this preparation contains 2 grains of 'maizenate of lithium.' From an examination made in this laboratory we are inclined to conclude that this statement is not in accordance with the facts. A search of chemical and pharmaceutical publications does not reveal that such a compound as 'maizenate of lithium' has ever been isolated and described, and we are very much inclined to

question its existence. We should be pleased to receive from you any evidence which you may care to send in substantiation of your claim in regard to the content of 'maizenate of lithium' in Maizo-Lithium — particularly a specimen of 'maizenate of lithium' or the method by which it is produced."

While this letter was sent Oct. 13, 1914, no evidence has been submitted up to date (January, 1915) to substantiate the asserted presence of maizenate of lithium in Maizo-Lithium.

The report just given shows that the manufacturer has found it expedient to surround his worthless nostrum with a cloak of mystery. A discussion of the jumble of uncritical claims, baseless assertions and evident falsehoods presented in favor of Maizo-Lithium would seem a waste of time when the secrecy of this nostrum is all-sufficient for its condemnation.

RECOMMENDATION

It is recommended that Maizo-Lithium be held in conflict with Rule 1 because its composition is kept secret; with Rule 4 in that it is exploited in a way to encourage its indiscriminate use by the public; in conflict with Rule 6 in that unwarranted therapeutic claims are made for it.

[EDITORIAL NOTE.—When the Council on Pharmacy and Chemistry was started we announced that we did not see any clear line of demarcation between "patent medicines" and many so-called "ethical proprietaries." Time has not caused us to change our opinion. As we have already shown, and as we shall have occasion to show in the future, not a few of the "ethical proprietaries" offered to physicians are being advertised by those who are pushing the rankest of "patent medicines." The three preparations mentioned above are sold—and presumably manufactured—by Mr. Ballard, of St. Louis. Mr. Ballard is the promoter of Ballard's Snow Liniment, Brown's Iron Bitters, Herbine, Dr. Herrick's Vegetable Liver Pills, Swaim's Panacea, Renne's Pain Killing Oil, etc. He is also the promoter of Campho-Phenique, exposed in THE JOURNAL some eight years ago.[1] The spectacle is not an edifying one. A manufacturer with one hand offers the public a profusion of cure-alls, while with the other he endeavors to foist on the medical profession preparations which are just as fraudulent. Some day our profession will awake to the disgrace of it all. It will also awake to the fact, which should have been evident ere this, that the nostrum business would cease if physicians

1. THE JOURNAL A. M. A., April 20, 1907, reprinted in "Propaganda for Reform," 8th Edition.

would refuse to accept into their offices, even as a gift, the nostrum-promoting medical journals that live off this trade. Fraudulent "patent medicines" will continue to thrive just so long as newspapers will publish "patent medicine" advertisements; fraudulent "ethical proprietaries" will continue to exist just so long as medical journals will advertise such proprietaries. As the better class of newspapers are rejecting "patent medicine" advertising on their own volition, so are the better class of medical journals rejecting advertisements of fraudulent proprietaries. Some newspapers will continue to carry nostrum advertising until their subscribers raise a protest that will cause the business department to take notice; so, too, some medical journals will continue to share the profits with the nostrum exploiters until an outraged medical profession repudiates such publications.]

SANMETTO

Report of the Council on Pharmacy and Chemistry

(From The Journal A. M. A., March 13, 1915, p. 926)

The following report on Sanmetto (Od Chemical Company, New York) has been adopted by the Council on Pharmacy and Chemistry, which authorized its publication.

W. A. PUCKNER, Secretary.

Sanmetto is one of the oldest proprietaries on the market. Its advertisements have been familiar to the readers of medical journals for several decades past. It is a typical nostrum. It is secret although the promoters have published various "near-formulas." The following are some of the statements regarding composition:

"A Scientific Blending of *True* Santal and Saw Palmetto with Soothing Demulcents in a Pleasant Aromatic Vehicle."

As this did not disclose the identity of the demulcents or the quantity of the alleged active constituents, the "formula" was, of course, meaningless.

Again it is:

"A Scientific blending of *true* Santal and Saw Palmetto in a pleasant aromatic vehicle."

Here the reference to "soothing demulcents" is omitted. The information furnished physicians at the present time is:

"It is a blend of harmonizing drugs."

A letter from a physician requesting information as to the exact composition of Sanmetto recently elicited the following reply:

". . . Sanmetto is a blending of true santal and saw palmetto with soothing demulcents in a pleasant aromatic vehicle. The demulcents are introduced not only for the purpose of modifying the irritant properties of the santal, but to add distinctively to the soothing properties of the finished product upon the mucous membrane of the urinary tract, and are not mentioned in our published formula for the simple fact that if we gave them, then we would do the advertising and the substitute manufacturer would engage in the 'unfair competition' of putting on the market his concoction, claiming to be made exactly after our formula, without spending a cent for advertising, relying upon our propaganda work to sell his substitute, although not the same article as nor equivalent to Sanmetto, from the fact that he would be working in the dark as to the processes in the manufacture of our product. There is no mineral substance in Sanmetto, nor any other ingredient that is detrimental in any way whatsoever. . . .

"OD CHEM. CO.,

"M. Haman, Pres't."

THE VALUE OF SANTAL AND SAW PALMETTO

The foregoing warrants the assumption that the active ingredients of the mixture are sandalwood oil and saw palmetto.

There was a period when the internal treatment of gonorrhea had a marked vogue. Balsamic remedies received the approbation of the medical profession as the most specific of internal remedies for this disease. As a representative of this class, sandalwood oil was very highly esteemed and had great popularity. As in other similar instances, this popularity was commercialized and the drug became the basis of many secret or semisecret mixtures, including "specialties" of pharmaceutical houses.

Sabal or saw palmetto is an official drug which at one time was used in genito-urinary affections, but now is seldom used, presumably because it has been found practically worthless. It is not mentioned by most pharmacologists, and those who do mention it regard it as of doubtful value. It is included among the preparations recommended for deletion as given in the report of the Committee on the Pharmacopeia of the American Medical Association (THE JOURNAL, Sept. 4, 1909, p. 792).

Even granting that sandalwood oil and saw palmetto do have therapeutic value, no one would think of regarding either or both of these preparations as of use except in inflammatory conditions of the genito-urinary tract, especially gonorrhea.

If one is to believe the advertisements, however, the combination of these drugs in Sanmetto is a wonderful medicine. One might even conclude that there are few conditions in which it cannot be given with profit. For instance:

"In Nervous Diseases, especially Neurasthenic cases with origin in some sexual or genito-urinary disorder, for its action as a vitalizing tonic and reconstructive, restoring nutrition to germ plasm, relieving pathological conditions and for soothing and sustaining the nerves controlling the parts."

Bear in mind in reading the foregoing statement and the following that we are concerned with two drugs whose effects are exerted on mucous membranes especially of the genito-urinary tract.

"In Gestation Cases, showing tendency to albumin and convulsions, for toning the pelvic organs, clearing up the urine and cleansing the urinary bladder and outlet. In the Lying-in-Room for relieving the affections of urethra and bladder, painful strangury of the urethra and painful micturition due to the pressure of fœtal head upon the neck of the bladder and upon the urethra during labor, and infection, either septic or gonorrheal."

"In Weakness of the Kidneys, causing loss in tone and general health and Impairment of Eyesight—for strengthening the kidneys and bladder and toning the nervous system; and also for aiding in the constitutional treatment of Gonorrheal Infection of the Eyes.

"In the treatment of the Prostate, Testes, Mammæ, Ovaries, and Urethra, Kidneys and Bladder, for its soothing, slightly antiseptic, aphrodisiac, toning and restoring action to the mucous membrane and glands. By its use the parts affected in many cases returning to their normal condition."

While the reference to its aphrodisiac action and to the restoration of parts to the normal may have little interest to physicians, it may be counted on to appeal to the sexual neurasthenic. In premature senility:

"Sanmetto . . . is unexcelled as a vitalizing tonic to the withered glands of the reproductive system, promoting their normal secretory activity."

These claims are not only absurd but also harmful; they tend to perpetuate a hypochondriacal state of mind in the class of patients appealed to—the sexual neurasthenic. There is, however, a more serious side; the tendency of certain other claims made for the preparation are vicious and dangerous as well as misleading. The advertising claims are likely to induce some physicians—those who accept advertising "literature" as dependable—to belittle the importance of serious diseases of the sexual organs and to be content with Sanmetto, which, even if it gave as good results as other balsamic remedies, would be, at best, only a halfway measure. Thus in an advertising pamphlet physicians are given this advice as to the treatment of gonorrhea.

"To provide the needed rest the patient should be instructed to simply keep the parts clean with warm water for the first week and let the discharge continue until you can control it by internal medication. I wish to emphasize the fact that there is no way that any acutely inflamed portion of the genito-urinary tract can get the rest required

so completely as by administration of Sanmetto. . . . After the acute gonorrhea has begun to subside the Sanmetto should be aided by mild astringent injections."

If there is any well-established fact in medicine, it is that gonorrhea is a serious disease—serious alike to the sufferer and to the community—and one which needs careful attention from the very first. To claim, either directly or by implication, that it can be cured by such a mixture designed to act on the kidneys, bladder and nervous system is false and dangerous doctrine.

The physician who prescribes Sanmetto prescribes a secret medicine for conditions which he is presumably competent to treat with simple remedies of which he knows the origin and action and which he can vary to suit the needs of the individual.

Sanmetto is a secret nostrum the exploitation of which is an invitation to haphazard, uncritical therapy and a menace to public health.

NEURILLA

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., March 27, 1915, p. 1093*)

The following report was adopted by the Council. Its publication was authorized to show how a practically worthless mixture may be exploited by means of ill-considered testimonials.

W. A. PUCKNER, Secretary.

Neurilla, which appears to be the sole product of the Dad Chemical Company, New York, is advertised as

"The Ideal Nerve Calmant."
". . . a nerve tonic . . . indicated in cases where the nerve centers are poorly nourished and over-sensitive . . ."
". . . a stimulant to the nervous system."
"A Valuable Aid in the Treatment of Fevers, Colds, La Grippe, etc."

The following non-quantitative and indefinite formula is given on the label of a recently purchased bottle of Neurilla:

"Prepared from Scutellaria Lateriflora, Passiflora Incarnata and Aromatics."
"Proportion of Alcohol 20.3%.
"Made by Dad Chemical Co., New York, U. S. A.
"Dose, One Teaspoonful Four Times a Day."

According to the formula, then, this mixture contains, aside from alcohol and aromatics, two vegetable drugs, scutellaria and passiflora, on which the alleged virtues of the preparation must be presumed to depend.

Scutellaria lateriflora, or skullcap, is a bitter drug, one of the many "herbs" to which, on wholly unreliable "clinical evidence," therapeutic properties were at one time ascribed. Most pharmacologists do not mention the drug, and those who do generally state that it has very feeble therapeutic properties. It was admitted to the Pharmacopeia, but in 1909 its deletion was recommended by a committee of the Section on Practice of Medicine of the American Medical Association (THE JOURNAL A. M. A., Sept. 4, 1909, p. 792). We understand that the next edition of the Pharmacopeia will omit mention of skullcap.

Passiflora incarnata, or passion-flower, is another "herb," which, although known for about seventy years, has never gained the confidence of the medical profession and has not even been admitted to the Pharmacopeia. According to a Council Report:

"None of the evidence is sufficient to show that passiflora has therapeutic value; hence it is deemed inadvisable to include the drug in the list of nonofficial remedies" (THE JOURNAL A. M. A., March 19, 1910, p. 983).

On these two obsolescent "herbs," then, rest the remarkable claims made for Neurilla. A certain degree of appetizing effect may be expected from the bitter taste and a very slight degree of physical stimulus from the alcohol. Except for these effects—and they are largely delusive and temporary—the preparation is therapeutically inert and worthless.

The evidence on which the manufacturers of Neurilla base their therapeutic claims appears to consist of testimonials from physicians. As a matter of fact, this is true of practically all of the large group of nostrums of which Neurilla is typical. An analysis of these Neurilla testimonials brings out clearly what such "evidence" is worth.

ILL-CONSIDERED TESTIMONIALS

The testimonials for Neurilla have been given with reference to indefinite conditions of nervousness that border on the psychic and include hysteria, neurasthenia, neuralgia and the like. Nervousness and indigestion are two diseases in which suggestion, especially when aided by bitters and alcohol, produces temporarily a feeling of improvement. As an illustration, take the following testimonial:

"But more striking was the following case: One evening between 5 and 6 o'clock I was sent for, family lives near me, and I was informed that the young lady had promised to be bridesmaid, a function she had never performed. Her mother said the daughter would certainly

drop in her tracks as she walked up to the altar with the procession, and they had about concluded to send a note saying to the parents of the bride that she could not come, although that would be very disagreeable (and no less offensive, said I). They agreed with me. I ordered Neurilla for two hours. She went to church, and, I was informed the next morning, passed through the dreaded ordeal simply fatigued, and was now fast asleep on account of the nice effect of Neurilla."

It might provoke a smile to think that a manufacturer would publish so silly a testimonial were it not that the very fact of its publication indicates that there are medical men thoughtless enough to read and accept such stuff as reliable evidence as to the value of any product.

TESTIMONIALS GIVEN LONG AGO—THE REMEDY ABANDONED

A number of physicians who had given testimonials were asked in writing whether the testimonials were genuine and whether they still entertained the high opinion of Neurilla expressed at a former date. Several replied that, if they had ever given such testimonials, they had forgotten the circumstance. From the replies received we select the following:

The testimonial which bears Dr. A's name reads:

"I am using Neurilla with most satisfactory results."

Dr. A now says:

"As to its positive value as a therapeutic agent I have not used it enough to know . . . If the language you quote . . . appears as given in or as a 'testimonial' it must in some way be garbled and appears wholly without my knowledge or consent."

Dr. B is quoted as having written:

"I do not often lend my influence to furthering the fame of a proprietary remedy, but I have achieved such excellent results from the use of Neurilla as a calmative in hysteria and other nervous disorders, that I feel its manufacturers are entitled to an acknowledgment of gratitude from me."

Dr. B writes:

"I have not prescribed a dose of the nostrum in years. The use of my name in connection with Neurilla is unauthorized."

Dr. C once wrote:

"I have used Neurilla with good results."

Dr. C now writes:

"In re 'Neurilla' I think I used the preparation once or twice and it seemed to do good work, but if due to the preparation or other influences, I am not able to verify. I have not used it since nor will, as I am opposed to using these preparations except in certain cases where the ℞ contains remedies whose value I have verified under the most rigid tests.

. . . . . .

"P. S. This testimonial must have been given many years ago."

Dr. D's testimonial is admitted to be based on a single case:

"I am using Neurilla in a bad case of neuralgic tic with very good results on an aged lady. She has taken several bottles, and is still taking it with very good results."

Dr. D sums up his later experience by saying:

"I have long since abandoned the use of Neurilla in practice."

The following bears Dr. E's name:

"I endorse Neurilla without hesitation. It meets all indications for which it is intended."

This is what Dr. E writes now:

"As to the enclosed testimonial in regard to Neurilla said to be written by me I have no recollection. I am not prescribing Neurilla."

Dr. F's experience is similar. The testimonial credited to him reads:

"I have prescribed Neurilla in nervous disorders with good results."

Dr. F now writes:

"I don't remember of ever having prescribed 'Neurilla' or of having given a testimonial for it or any other patent medicine if I knew it to be so."

SUMMARY

In the booklet from which the foregoing are taken, there are forty testimonials. Those which we quote are merely samples. To sum up the results of this analysis: Of the testimonials some are said to be unauthorized; a number were written with so little thought that the writers had since forgotten their very existence; the conclusions expressed in most are not in fact justified by the writers' mature judgment and experience. A number of writers admit that their experience is insufficient to determine whether the supposed good results were due to the medicine used or to other influences. Of course such evidence is unworthy of credit and happily, very little is now being furnished by doctors; even our courts refuse to admit it.

In short, the published formula shows that Neurilla is nothing more than a preparation of discredited drugs; it is exploited largely by means of carelessly formed and thoughtlessly expressed opinions of physicians. It is recommended that this report be published as an illustration of such methods and as a protest against them.

[EDITORIAL COMMENT.—Neurilla is advertised in the following publications:

Archives of Pediatrics,
Atlanta Journal Record of Medicine,
Charlotte Medical Journal,
Indianapolis Medical Journal,
International Journal of Surgery,
Journal of Nervous and Mental Diseases,
Medical Herald,
New York Medical Record,
Medical Review of Reviews,
Medical Sentinel,
Medical Standard,
Pacific Medical Journal,
Southern Practitioner,
Texas Medical Journal,
Woman's Medical Journal.
Eclectic Medical Journal,
Ellingwood's Therapeutist,
Journal of the American Institute of Homeopathy.]

PEACOCK'S BROMIDES AND CHIONIA

Reports of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., April 3, 1915, p. 1177*)

The Council has authorized publication of the following reports on Peacock's Bromides and Chionia, sold by the Peacock Chemical Company, St. Louis.

W. A. PUCKNER, Secretary.

PEACOCK'S BROMIDES

This is another nostrum of the ordinary mixture type. Of the various statements concerning composition furnished by the company, the following gives as much information as any:

"In Peacock's Bromides it is designed to unite fifteen grains of the purest bromides of Potassium, Sodium, Ammonium, Calcium and Lithium, in such proportion as to insure the bromine equivalent of potassium bromide. Each fluid drachm about equals, in medicinal strength, fifteen grains of potassium bromide."

The label on the trade package indicates the presence of 10 per cent. of alcohol. It will be observed that the proportions of the different bromids are not stated. Hence, the assertion of the Peacock Chemical Company that "there is nothing secret in this compound" cannot be true. A physician prescribing it cannot know how much of each ingredient he is giving; it may be 14½ grains of potassium bromid and ⅛ grain each of sodium, ammonium, calcium and lithium bromid, or any other of an enormous number of possible permutations of the proportions.

While the theoretical basis of bromid medication is not yet fully settled, the weight of the best pharmacologic

authority and clinical experience is decidedly against the dogmatic claim of the Peacock Chemical Company that "the best result is obtained by prescribing a combination of bromides." And if there were any advantage in prescribing such a combination, the physician ought to regulate the proportions.

The following quotations are from the advertising matter:

"Being uniform in purity and therapeutic power, it can be relied upon to produce clinical results which it is believed cannot be obtained from the use of commercial bromide substitutes."

"The purity, quality and constant uniformity of this high grade product have long made it a standard bromide preparation."

These claims are unfounded. The analyses published in the concern's own advertising "literature" show a variation of 8 per cent., in the bromid content, which certainly indicates a sufficient lack of uniformity.

Again quoting:

"In order to insure the best results the bromides must be pure, i. e., free from alkalies and almost free from chlorides. The U. S. P. allows three per cent. of chlorides. Peacock's Bromides contains the least possible amount of this impurity. Bromism is therefore less frequent in those cases in which this preparation is employed."

In view of the claim of low chlorid content, it is interesting to note that the analyses above referred to show that the chlorid content is actually higher than that of some other bromid preparations on the market.

The claim of merit on the ground of freedom from chlorids is, of course, absurd, and must be regarded as an attempt to play upon the credulity of the doctor. As a matter of fact, the average individual takes with his food many times the amount of chlorid he could possibly take in contaminated bromid. The 10 per cent. of alcohol would undoubtedly have a greater disturbing influence on the bromid action than the amount of chlorid that might be present in any bromid on the market.

Then we have the statement that, owing to this freedom from chlorids:

"Bromism is therefore less in those cases in which the preparation is employed."

Sodium chlorid, even as an impurity, would retard rather than favor the development of bromism; sodium chlorid is even used as an antidote in bromid poisoning.

The therapeutic claims lay stress on the value of the bromids in sleeplessness, epilepsy, sexual excitement, tetanus, infantile convulsions, chorea, delirium tremens, the climac-

teric, migraine, headache due to pelvic conditions, ovarian neuralgia, etc. These and other claims, while too vague to be branded as falsehoods, are misleading and not in accordance with modern teaching or practice; the latter recognize the limitations of bromid therapy as well as its scope and advantages. For instance, in epilepsy the company asserts that:

"Large doses must be given if we expect to control the convulsions. We are to be guided by the frequency and the severity of the seizures, the saturation of the system by bromides and by the age of the patient. The rule is 'large doses for long periods but with occasional periodic monthly or quarterly omissions.' When we have succeeded in controlling the convulsions in so far as greatly diminishing the frequency and severity of the attacks we may then attempt to decrease the dose, but the results must be carefully watched. Increase in frequency of convulsive seizures is a sign that the bromides must again be pushed as before."

The best modern clinical teaching concerning the treatment of epilepsy is that bromids should be avoided except as a last resort. Bromids do not cure, and the amount necessary to control the convulsions may produce a degree of mental hebetude that is a greater evil than the disease itself.

It is recommended that the preparation be held ineligible for admission to N. N. R., because of its conflict with Rules 1, 4, 6 and 10 of the Council, and that this report be published.

CHIONIA

Chionia, according to the statement of the Peacock Chemical Company, which exploits the product, contains 19 per cent. alcohol and is "A Preparation of Chionanthus Virginica."[1]

This preparation is advertised particularly as "a potent hepatic stimulant" and special claims are made for it in various disturbances of the liver:

"Chionia is very well adapted in the treatment of hepatic congestion owing to its specific action in depleting the portal circulation."

In passive congestion of the liver, the manufacturers would have us believe

". . . we have a drug in Chionia that will stimulate the circulation of the blood and lymphatics of the liver as well as stimulate its physiological activities and instead of the patient vomiting the blood an internal depletion of the liver occurs."

1. Of Chionanthus Virginica or fringe-tree, the Council on Pharmacy and Chemistry in its 1912 report on "Some Unimportant Drugs" said: "The drug is much used by eclectics and homeopathists, especially as a depurant in hepatic and syphilitic disorders . . . The claims for this remedy are not supported by experimental evidence and clinical reports of its use fail to show indications of discriminating critical observation. It is not noticed by most pharmacologic authorities."

". . . in cases of simple jaundice due to circulatory (congestive) changes in the liver, Chionia is the drug 'par excellence' that will rapidly cause a disappearance of this symptom."

As a prophylactic against eclampsia, if a history of torpidity of the liver is obtained:

"CHIONIA should be used during the major portion of child-bearing period because it acts directly on the liver stimulating its functional activity."

Chionanthus virginica has never been shown to have the slightest pharmacologic activity and no evidence is presented that its offspring, Chionia, has any therapeutic value whatever in any disturbance of the liver. The promoters themselves indicate a lack of faith in their own preparation, for they advise the use of old and efficient forms of treatment along with Chionia—heart tonics and laxatives in passive congestion of the liver, mercurial purge or podophyllin and sodium phosphate in "biliousness," and quinin in malaria. Finally, with delightful English and elaborate insouciance, they advise in the treatment of eclampsia:

"In all cases the uterus should be emptied as quick as possible. (Version of Cæsarian Section.)"

The physician who prescribes Chionia promotes a fraud. The Council held Chionia ineligible for admission to N. N. R.

[Editorial Comment: In Peacock's Bromides and Chionia the Peacock Chemical Company has, for a third of a century, been foisting on the medical profession nostrums composed of drugs that are easily combined in any proportion that the physician may want to prescribe. The company has been inflicting on the unthinking physician pseudoscientific rubbish in the form of advertising literature that should long ago have been regarded as an insult to the intelligence of the medical profession. The following medical journals are carrying advertisements of Peacock's Bromides and Chionia:

Alienist and Neurologist
American Journal of Surgery
American Medicine
Archives of Pediatrics
Atlanta Journal-Record of Medicine
Buffalo Medical Journal
Charlotte Medical Journal
Chicago Medical Recorder
Denver Medical Times and Utah Medical Journal
Eclectic Medical Journal
Ellingwood's Therapeutist
Indianapolis Medical Journal
International Journal of Surgery
Lancet-Clinic
Louisville Monthly Journal of Medicine and Surgery
Maryland Medical Journal
Medical Brief
Medical Fortnightly
Medical Herald
Medical Record
Medical Review of Reviews
Medical Sentinel
Medical Standard
Medical Summary
Medical Times

Medical World
Nashville Journal of Medicine and Surgery
New Orleans Medical and Surgical Journal
New York Medical Journal
Pacific Medical Journal
Southern Practitioner
Texas Medical Journal
Texas Medical News
Therapeutic Gazette
Wisconsin Medical Recorder
Woman's Medical Journal]

CHEMOTHERAPY AND TUMORS*

Richard Weil, M.D.
NEW YORK

(*From The Journal A. M. A., April 17, 1915, p. 1283*)

Within the last three years a number of reports have appeared in the medical press which bear on the treatment of malignant growths in human beings by chemical preparations. The most persuasive and the most insistent claims have been made in connection with the colloidal solutions of certain metalloids and metals, notably selenium, vanadium and copper. At the same time a number of drug houses both in this country and abroad have placed on the market proprietary preparations of these substances in various forms, for which the claim is made that they produce striking therapeutic effects and sometimes even cures in malignant neoplasms.

The impulse toward the use and production of this type of preparation is directly traceable to a series of scientific experiments on the tumors of animals, which date back no farther than the year 1911. In that year Wassermann and his co-workers[1] published a report on the treatment of rat tumors by means of the intravenous injection of selenium compounds. This paper received wide notoriety through its enthusiastic diffusion by the lay press. Shortly afterward Neuberg and his co-workers[2] published their observations upon the therapeutic effects of certain metallic compounds. The clinical application of the encouraging results obtained by these authors in animal tumors followed rapidly, and up to the present time a number of papers have appeared in which the claim is made that human tumors also may be favorably influenced through the constitutional use of sub-

* From the Cancer Research Service of the General Memorial Hospital, New York.

* This critical discussion of the status of chemotherapy in tumors was prepared at the request of the Council on Pharmacy and Chemistry of the American Medical Association.

1. Wassermann, Keysser and Wassermann: Deutsch. med. Wchnschr., 1911, p. 2389; Berl. klin. Wchnschr., 1912, p. 4.

2. Neuberg and Caspari: Deutsch. med. Wchnschr., 1912, p. 375. Neuberg, Caspari and Löhe: Berl. klin. Wchnschr., 1912, p. 1405.

stances similar to those used by Wassermann or Neuberg. In some cases, use has been made of colloidal solutions of the heavy metals such as copper; in others, selenium compounds have been used, while in a third set of observations the therapeutic agent represents an attempt to combine the virtues of these two types of therapy by employing selenium in colloidal form. As an example of the first class, may be cited the cuprase of Gaube du Gers;[3] of the second, the seleniovanadic ointment of Roemer and the sulpho-selene of Walker; of the third, seleniol and electro-selenium.

Inasmuch as this new type of cancer therapy derives its origin, its justification and its support, in very large measure, from the laboratory results obtained in animals, it is a matter of considerable importance to examine those results with care, in order to determine whether they furnish a satisfactory basis for human therapy, and whether they justify the hopes to which they have given rise.

It is safe to assert that the application of chemotherapy to the treatment of tumors practically dates from the publications of Wassermann. He stated the principle that a rational therapy of tumors must be based on constitutional treatment. It appears evident that local treatment can have only local effects. The lymphatic extensions of tumorous growths, and the often unsuspected metastases in distant organs must of necessity escape the effects of purely local treatment. Hence, Wassermann reached the conclusion that all treatment of cancer which was to be effective, and not merely palliative, must be carried to all parts of the body by means of the blood stream. He therefore introduced the use of intravenous injections in the experimental therapy of rat and mouse tumors. An accidental observation led him to believe that selenium was a substance possessing a high degree of affinity for tumor cells.

In order to insure the penetration of the tumor in the live animal by this substance, however, he considered it essential to combine it with some other highly diffusible substance. This type of substance, which was to act as a carrier of the selenium, he described under the name "cytotrochin," from the Greek word τροχιά, meaning road. For this purpose he selected eosin. The eosin and the selenium were then combined by a method and in a form the details of which have never been published. All that we know of this preparation is contained in the statement that it is very difficult to produce, and that it is extremely unstable and difficult to keep. Mice can be given amounts of from 2 to 3 mg. of this sub-

3. Gers, Gaube du: La cuprase et le cancer, Paris, 1913.

stance in solution. Wassermann experimented with mice inoculated with transplanted tumors of the types of carcinoma and sarcoma. After from three to five intravenous injections of the drug, he notes that the tumors become softer and fluctuate. After still further injections the fluid mass undergoes absorption, and the tumor gives the impression of an empty sac. If it is possible to carry the injections up to the number of ten or twelve, recovery ensues. In such cured animals there remain only the unabsorbed portions of the fibrous capsule. Recurrences were not observed in the cured animals. Wassermann further stated that two spontaneous tumors in mice which had been treated by this method presented favorable results.

Wassermann's original presentation gave few experimental details, and has not been followed by the promised scientific report. From his article it is impossible to determine what proportion of his animals were cured and what proportion failed to survive the treatment. From a later paper by Keysser[4] we learn that by far the larger proportion of the animals perished during the treatment in the stage of softening, so that a cure was accomplished in from only 3 to 5 per cent. of the animals. This is a point of great importance, inasmuch as it furnishes an indication of the highly dangerous character of this mode of treatment. Fatal results are attributed by Keysser to the absorption of toxic products from the tumor. This contention, however, is supported by no observations, and it is certainly equally fair to assume that death results from the toxic effects of the compound. A microscopic study of tumors taken from animals undergoing treatment was made by Hansemann. He found that the death of the cells was the result of nuclear destruction.

Within a very few months of Wassermann's publication, Neuberg and Caspari[2] published a paper which was the first of a series of studies on the therapeutic effects of the heavy metals on the animal tumors. They used zinc, platinum, tin, selenium, copper, silver and cobalt in the form of certain complex organic compounds, the composition of which is not revealed. Owing to the fact that intravenous injections of these compounds produced a specific effect on the tumors, they are described as "tumoraffin" substances. Immediately after the intravenous injection of these preparations, there followed a marked hyperemia of the tumor, whereas the remainder of the mouse's body appeared markedly anemic. The hyperemia was often attended by hemorrhage into the tumor. This first stage was succeeded by liquefaction and

4. Keysser: Wien. klin. Wchnschr., 1913, p. 1664.

absorption followed by recovery in favorable cases. The authors failed to state in what proportion of their experiments the animals died, and in what proportion recovery ensued.

The second paper on this subject is by Neuberg, Caspari and Löhe,[2] in which further details are vouchsafed. They state that with the compounds used by them the toxic and the therapeutic doses approximate very closely, from which it follows that the treatment, as with the Wassermann method, results in a very high mortality. Smaller doses produce no therapeutic effect; on the contrary, they seem to act as a stimulus to the tumor, accelerating the normal rate of growth. Spontaneous tumors show similar effects, but no cures are recorded. Only in tumors in which autolysis is active *intra vitam* does the method exert any effect. Consequently the benign primary tumors of animals, such as fibromas, are not influenced by it.

Neuberg and Caspari are to a great extent responsible for the colloidal theory of treatment in tumors. Accepting the observations of Petri and others that the autolytic ferments in tumors are quantitatively greater and qualitatively different from those present in the normal tissues of the body, they venture the assumption that the process of recovery in the experimental tumors of animals is due to the self-digestion of the tumor by these ferments. Ascoli and Izar[5] had shown that such ferments are materially stimulated by the presence of metals, and more especially of metals in colloidal form. This contention is apparently in harmony with the well-established fact that certain colloidal metals of themselves are capable of acting under certain circumstances as ferments. Neuberg and Caspari were at first of the belief that the compounds produced by them circulate in colloidal form. Subsequently they stated that these compounds were crystalline substances, but they assumed, under the influence of the theoretical consideration mentioned above, that these substances are broken up in the tumor and there undergo transformation into the colloid state.

In connection with the preceding observations there are certain other experimental results which require mention. Izar[5] succeeded in curing rat tumors by means of injection of colloidal sulphur. C. Lewin[6] cured subcutaneous mouse tumors with various preparations of gold. Werner and

5. Izar: Ztschr. f. Immunitätsforsch., 1913. Izar and Basile: Berl. klin. Wchnschr., 1913, p. 1312.

6. Lewin, Carl: Berl. klin. Wchnschr., 1913, p. 147; Berl. klin. Wchnschr., 1913, p. 541.

Szécsi[7] produced similar results through a combination of selenium-vanadium with cholin-borate; in these experiments the selenium-vanadium was supposed to be present in colloidal form.

Within a comparatively brief period of time, therefore, it fell to the lot of a number of observers, using strikingly different substances, to produce therapeutic effects amounting in a certain percentage of cases even to cure in the experimental tumors of the lower animals. The various procedures have little in common. Both metals and non-metallic substances have been employed either in colloidal form or in combination with organic radicals. In some instances a diffusible carrier is combined with the basic substances; in others not. All of the preparations appear to possess a high degree of toxicity, although adequate data on this very essential feature are almost invariably withheld.

Wassermann's results with eosin-selenium were soon critically examined by other observers. Uhlenhuth[8] and Contamin[9] were unable to confirm his observations, but their negative results are attributed by Keysser to the fact that they were not in possession of the proper formula for the preparation of the eosin-selenium compounds as used by Wassermann. Apolant,[10] however, in Ehrlich's name confirmed Wassermann's findings.

The most important critique of eosin-selenium has been contributed by the subsequent investigations of one of Wassermann's original collaborators, F. Keysser.[11] Keysser's publication contains a large number of very careful observations on the various forms of eosin supplied by the German manufacturers, as well as on other matters which cannot here be considered in detail. He finally reached the conclusion that the eosin furnished by the manufacturing house of Sandoz was the most effective for his purposes, inasmuch as it combined the lowest grade of toxicity with the highest capacity for discoloring the tissues. The selenium he used in the form of seleno-vanadium furnished by Clin of Paris, which was the identical preparation used by Werner and Szécsi in combination with borcholin. The maximum dose of this selenio-vanadium is 0.06 c.c. for each gram of mouse.

7. Werner and Szécsi: Ztschr. f. Chemotherap., 1913, Orig., i, 358. Szécsi: Ibid., ref., 1913, ii, 1060.

8. Uhlenhuth, Dold and Bindseil: Ref., München. med. Wchnschr., 1912, p. 1782.

9. Contamin, Detoeuf and Thomos: Bull. de l'assn. franç. pour l'étude du cancer, vi, 62.

10. Apolant, H.: VI Tag. der freien Vereinigung für Mikrobiologie., Berlin, 1912. Ref. München. med. Wchnschr., 1912, p. 659.

11. Keysser, F.: Ztschr. f. Chemotherap., 1914, Orig., ii, 188.

Eosin, 0.01 gm., dissolved in 0.5 c.c. of physiologic salt solution, is mixed with 0.5 c.c. of the selenio-vanadium. This mixture in then used for intravenous injections. The results produced by the injection of this mixture are to all intents and purposes similar to those obtained by Wassermann, except that Keysser induced cure in a larger proportion of animals, namely, from 6 to 8 per cent. It is evident from his careful description of his experiments that the treatment is extremely toxic to the animals. The therapeutic dose is considerably greater than one-half the toxic dose. This accounts for the fact that an extremely large proportion of the animals perish during the course of the treatment. The tumors failed to be influenced unless the dose given fell very little short of the fatal amount. Moreover, in order to accomplish a complete cure, at least eight to ten injections must be given, and in some instances not less than fourteen.

Keysser's most important conclusions, however, were obtained by following an altogether different line of procedure. It had been pointed out by Carl Lewin[6] that the therapeutic results obtained from subcutaneous mouse tumors, however encouraging, could not be logically applied to the treatment of human cancers. The subcutaneous transplanted tumors, as is well known, are as a rule limited by a distinct capsule and show no tendency to infiltrative growth. In this particular they present a most striking difference when compared with human tumors. On the other hand, the metastases of mouse tumors in the internal organs present an infiltrative mode of growth and thus approximate very much more closely to the human type of tumors. Keysser therefore determined to test the therapeutic effectiveness of his compounds on tumors implanted in various organs. He developed a technic which enabled him to implant tumors in the liver, the spleen, the kidneys and other parts of the mouse by means of injection through special needles, often without the assistance of a cutting operation.

The tumors so implanted grew rapidly, and within from two to three weeks reached the size of cherry pits. The growth was characteristically infiltrative. Animals with these tumors were then submitted to intravenous injection of the therapeutic agents in exactly the same fashion as the animals carrying subcutaneous tumors. The results, however, were absolutely different. Whereas the subcutaneous tumors invariably showed a much more intense discoloration than the other tissues of the mouse, this feature was entirely lacking in the case of the internal tumors. Softening and liquefaction, which almost invariably follows on the third or

fourth injection in the case of subcutaneous tumors, and which is the first symptom of cure, never presented itself in the case of the internal tumors. Their consistency throughout the treatment was indistinguishable from that of the tumors of control animals. The treatment, in fact, appeared to exercise not the slightest influence on internal tumors. There was neither cessation nor retardation in growth, but the tumors continued their normal rate of destructive increase with the production of metastases, leading eventually to the death of the animal either during the course of the treatment or shortly thereafter. Microscopic changes, such as had been observed by Hansemann in the case of subcutaneous tumors, were entirely lacking. No matter in what organ the tumors were implanted, these results remained the same. No matter what type of tumor was employed, whether carcinoma, adeno-carcinoma or sarcoma, the therapeutic outcome was regularly and consistently nil.

These results induced Keysser to determine whether or not eosin-selenium could actually be shown to exercise a deleterious effect on cancer cells outside the body. In order to do this he made a suspension of mouse tumor cells in salt solution and mixed this with the eosin-selenium-vanadium, using the latter in amounts equivalent to three times the fatal dose for a mouse. After the mixture had stood from one to three hours, it was injected either subcutaneously or intravenously into mice in order to test the vitality of the cells. In every instance the injections resulted in the production of tumors which could be in no way distinguished from the tumors produced by untreated cancer cells. In other words, the therapeutic preparation had absolutely no effect on the tumor cells.

In the same way Keysser carried out experiments along the lines inaugurated by Neuberg, using a combination of glycocoll and copper. He also tested the combination of borcholin with selenium-vanadium used by Werner and Szécsi. He was able to confirm the fact that both of these substances produced an unmistakable therapeutic effect on subcutaneous tumors. On the other hand, they were absolutely without influence on the internal tumors. In this respect, therefore, they were entirely comparable with the eosin-selenium compound. The theoretical basis constructed by Neuberg, which rests on the assumption that the metallic compounds stimulate autolytic processes in the tumors, was also subjected by Keysser to destructive criticism.

Finally, Keysser showed that none of these therapeutic agents were effective even in the case of subcutaneous

tumors, unless the latter had reached at least the size of cherry pits. If a therapeutic injection were made immediately after inoculation of the tumors, no effect was observed. The tumors grew exactly as in the control animals, and the injected animals died in about the same period of time as they.

All of these facts, which taken together constitute a very remarkable and convincing piece of scientific investigation, permit of but one conclusion. It is quite clearly established that none of the preparations of which the therapeutic effectiveness has hitherto been proclaimed exercise any direct influence on the life or development of the tumor. Under certain very definite and restricted conditions, however, they do appear to produce certain changes in the tumors, and in a small proportion even cures. These results, however, are obtained only in the case of tumors which are subcutaneous in location and not smaller than a cherry pit in size. Keysser's interpretation of the striking differences between the effects observed in the subcutaneous and in the internal tumors is of interest in this connection. He believes that the constant palpation and examination of the subcutaneous tumors, which is prompted by interest in the experiment, produces circulatory changes with hyperemia and hemorrhage. These circulatory changes are responsible for the increased tendency of the injected substances to lodge in the tumors, thereby possibly increasing the tendency to autolysis which the circulatory changes have inaugurated. It is, of course, questionable whether this explanation can be regarded as final. In a series of experiments which I performed many years ago, I was able to show that sodium iodid when injected intravenously accumulates in tumors in larger amounts than in any other tissue of the body in rats. A similar observation has been recorded by Wells, de Witt and Corper.[12] In the same way I found that various dyes, such as Congo red, when injected intravenously, could be demonstrated in tumors long after the rest of the body had recovered its normal color; the liver alone vied with the tumors in this respect. The dyestuff was invariably sharply localized in the necrotic portions of the tumor. The conclusion seemed obvious that, owing to circulatory conditions or possibly even to chemical conditions, the dye was retained longest in the necrotic parts of the tumor. This effect was unquestionably not due to handling, inasmuch as

12. Wells, H. G., De Witt, and Corper: Ztschr. f. Chemotherap., 1914, Orig., ii, 110.

the animals in my experiments were not palpated from the time of injection until death.

I have, however, had an even more striking demonstration of the same fact. I have given intravenous injections of dyes to patients suffering with various forms of internal tumors, as, for example, cancer of the breast, in the hope of favorably influencing the growths. At operation, the picture presented by the tumor is striking in the extreme. It presents areas of various size which are intensely discolored by the dye. These areas, both to the naked eye and under the microscope, are the necrotic parts of the tumor. The actively growing areas of tumor tissue and all the normal tissues of the organ present their normal color. All of these observations lead to the conclusion that the necrotic areas in tumors either possess a higher affinity for sodium iodid and for the dyes than do the normal tissues, or that these substances are more slowly absorbed from the necrotic areas owing to the circulatory deficiency. Whichever of these explanations be accepted, it is quite reasonable to believe that necrotic areas might well undergo liquefaction under the influence of the various substances which have been used for therapeutic injection. Such a result is, of course, without direct effect on the growth or vitality of the living part of the tumor. This fact is quite clearly evidenced by the experimental data, which show that the internal portions of the tumor might undergo liquefaction and yet the tumors were not cured. Indeed, Löhe, who made microscopic examinations of the tumors treated by Caspari and Neuberg, states particularly, with reference to a tumor which had been subjected to treatment, that "the central portion of the tumor showed softening, while the external margin was composed of actively growing cells." The central portions of implanted tumors are, of course, those which first undergo spontaneous necrosis.

It still remains to explain the small percentage of cures achieved by Wassermann and by Keysser. It does not appear to me that this problem presents any insuperable difficulties. The fact must be emphasized that practically 95 per cent. of the animals die under the treatment, which sufficiently indicates the toxic effects of the agent used. We must remember that transplanted tumors are under all circumstances at a certain disadvantage as compared with the normal tissues of the body. After all, they are implanted on a foreign soil. Their blood supply is impoverished and imperfect. They have a natural tendency to undergo necrosis, and in many cases spontaneous retrogression. It is not strange, therefore,

that they should prove in slight degree more susceptible to toxic effects than are the normal tissues of the body.

If we remember that the various therapeutic agents introduced in all probability reach a somewhat higher degree of concentration in the necrotic areas of the tumor than in the normal tissues of the body, an assumption which is entirely in accord with the facts as observed in the case of sodium iodid and of various dyes, we may be quite prepared to believe that this factor is sufficient to induce the destruction of the marginal healthy and living cells of the tumor. The fact that small subcutaneous tumors were found by Keysser to be entirely refractory to the treatment is entirely in accord with this assumption, in view of the fact that tumors of this size present practically no central necrosis. The same explanation holds of the observation previously cited from Caspari that the primary spontaneous tumors of animals do not yield to the treatment. Indeed, he himself states that the treatment is effective only in tumors in which autolysis takes place during life. The word autolysis, however, in this connection is a misnomer and represents a gratuitous assumption; as an actual fact, one is entitled to say only that such tumors undergo central necrosis, in all probability owing to defective circulatory supply. The process is exactly similar to the coagulation necrosis described in the case of tubercles by Weigert. If autolysis occurs it is only secondary to the preceding necrosis.

This explanation, however, is confronted by the fact that the internal tumors produced by Keysser showed no tendency to effect a localization of the dyes, and correspondingly no tendency to be affected by the therapeutic agents. One might be permitted to inquire whether these internal tumors had undergone any necrosis. Keysser unfortunately makes no mention of this matter. It is certainly true that the infiltrative mode of growth of the internal tumors, which is entirely different from that of the subcutaneous implantations, is associated with a much better blood supply and a lessened tendency to undergo necrosis. That such tumors can undergo necrosis, however, is evidenced by certain illustrations given by Carl Lewin in his paper on internal tumors. But such changes usually occur only in advanced stages. To judge from his plates, Keysser worked with relatively small tumors, an assumption which is rendered even more likely by the fact that his injections were undertaken in a fairly early stage of their growth. In this connection I may quote certain experiments of my own on internal tumors.* The

* Jour. Med. Research, 1913, p. 497.

implantations made in my experiments were produced by intravenous injections of a tumor suspension into the jugular vein of rats. Such injections resulted almost invariably in the production of a large number of tumors in the lungs, which, as is well shown in the figures accompanying the original article, differed very markedly in size. The smaller of these tumors are composed throughout of actively growing cells, while the large tumors present an area of central necrosis exactly as do the subcutaneous tumors. If such an animal be given an intravenous injection of a dye such as Congo red, it will be found that the larger tumors present an area of central discoloration corresponding to the area of previous necrosis, while the smaller tumors, like the normal tissues, are not colored. Thus, it is clear that the internal tumors implanted in animals are subject to the same laws concerning the distribution of dyes and, of course, other substances as are the subcutaneous tumors. As I have stated previously, an exactly analogous observation has been made in a human breast tumor. In the absence of any contradictory evidence, therefore, I think that it is perfectly justifiable to assume that Keysser failed to achieve a result in the internal growths simply owing to the fact that those growths presented practically no areas of necrosis at the time of his injections.

Another theoretical question which bears closely on the recent therapeutic investigations in human beings concerns the rôle of colloids as such in the procedure. It is quite clear from what has already been said that all experiments with animal tumors have been largely influenced by the belief that metals in the colloidal form exercise a peculiar and characteristic influence on the destruction of tumors. Even where the therapeutic agents have been introduced in crystalline form, as by Neuberg and Caspari, the authors find themselves compelled to assume that the metals are reduced to colloidal form within the tumors. For the latter assumption there is absolutely no evidence; it is due simply to the influence of the colloidal theory. If one critically examines the data on which this theory is based, one is forced to the conclusion that it has practically no established claim to validity. If we grant that colloidal metals have been shown to stimulate autolysis in the test tube, the same fact must be admitted of metals in noncolloidal solution. The experiments, however, are very far from establishing either of these facts satisfactorily. But even were this the case, it is an unjustifiable inference that living tumor cells would be influenced in anything like the same manner as are the dead

cells observed in test-tube experiments. As an actual fact, we know from the work of Evans and Schulemann that only the "scavenger cells" of the body take up foreign colloids, and to this class the tumor cells do not belong. Moreover, the form in which metals are introduced into the circulation is not necessarily or even probably the form in which they act on the tissues. Colloidal solutions of the metals are certainly subject to precipitation and other changes on entering the blood. This fact I have shown experimentally in a previous study on colloidal copper.[13] In the same way it is probable, as has been pointed out by Wells, that metals when introduced in crystalloid form may rapidly be altered so that they are carried throughout the body in colloidal form. All of these considerations indicate how unjustifiable is the assumption that colloidal metals exercise a peculiar action on growing tumors. It is hardly surprising that their empiric use has failed to measure up to expectations based on so slim a foundation of fact.

CLINICAL OBSERVATION

Clinicians have not been slow in following the lead suggested by the therapeutic experiments in animals. It is perfectly proper that this should be the case. In dealing with a disease of the character of cancer, in many instances entirely beyond our power to influence, no one can question the advisability of trying any and every agent which holds out the slightest promise. Unfortunately a closer analysis of the animal experiments fails to vindicate even that degree of faith. When one considers the facts which have been analyzed in the preceding discussion, it would appear not only futile but actually dangerous to attempt to benefit cancer sufferers by means of any of the agencies which have been employed in animal experimentation. Nevertheless, the fact remains that a variety of preparations have been used in the human clinic. The various types of preparations may be satisfactorily grouped under four classes, namely:

1. The crystalline salts of selenium.
2. Selenium in colloidal solution.
3. Other metals in colloidal solution.
4. Compounds of metals with organic radicals.

These substances have been administered by injection or by the mouth. In the case of injection, the injections have been made either into the subcutaneous tissues, intramus-

13. Weil, Richard: The Effects of Colloidal Copper with an Analysis of the Therapeutic Criteria in Human Cancer, *The Journal A. M. A.*, Sept. 27, 1913, p. 1034.

cularly, or intravenously, or finally, directly into the tumors. Before passing to a further consideration of this subject in detail, it may be well to recall the fact that in the experimental tumors of animals, no matter what preparation has been used, it has been possible to accomplish therapeutic effects only by the use of relatively enormous doses of the medicament, of doses, in fact, which were scarcely lower than the lethal dose. Certain experimenters have noted that smaller doses actually stimulated the growth of the tumors. In the second place, it has almost invariably been found necessary to administer the treatment intravenously, inasmuch as the other modes of administration failed of therapeutic effect. It is quite apparent that a procedure in human beings in any degree analogous to that pursued in animals is entirely impossible. The doses used, with one notable exception to be subsequently mentioned, have invariably been relatively small. Hence it is apparent at the outset that at least one fundamental condition of success in the treatment of animal tumors has been necessarily excluded in the clinical applications.

The salt used by Wassermann is not stated in his original publication. Wolff[14] speaks of it as a sodium salt, whereas Keysser says that it was a combination with potassium cyanid. In only one instance, as far as I am aware, has the sodium salt been used therapeutically in human beings. Delbet[15] states that he employed this salt intravenously in one case, and that its use was shortly followed by death. Unquestionably the salts of selenium are very much too toxic to be used in this way.

The majority of those who have worked with selenium have used it in colloidal form, either preparing it themselves or employing one of the preparations put on the market by the pharmaceutic firms. Of the latter the best known are the electro-selenium of Clin, and the Seleniol of Couturieux. Of those who have made use of selenium in these forms may be mentioned Cade and Girard,[16] Bougeaut and Galliot,[17] Blumenthal,[18] Thiroloix and Lancien,[19] Delbet, Laurent and

14. Wolff: Die Lehre von der Krebs Krankheit, iii, b, 1913.
15. Delbet, P.: Bull de l'Assn. franç. pour l'étude du cancer, 1912, v, 121; ibid., 1913, vi, 85.
16. Cade and Girard: Bull. Soc. méd. d. hôp. de Lyon, 1912, xi, 397.
17. Bougeaut and Galliot: Clinique, Paris, 1912, vii, 501.
18. Blumenthal, A.: Jour. méd. de Bruxelles, 1912, xvii, 325; Presse méd. belge, 1913, lxv, 919.
19. Thiroloix and Lancien, A.: Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, xxxiii, 197.

Bohec,[20] and most extensively of all, M. Touche.[21] All of these authors have described cases of malignant new growths of the most varied character which were treated by these preparations.

The results obtained are fairly concordant. The intravenous injection of the preparation produces but slight disturbance. There is leukocytosis, a moderate rise of temperature, and not infrequently a chill. Otherwise the substance seems to possess no toxicity. The effects produced on the tumors have almost invariably been described as encouraging. Touche, who treated twenty-seven cases in this way and has described each case in detail, states that under the treatment the surface of the tumors, if ulcerated, became cleaner and healthier; the tumors became softer; the rate of growth was arrested, and there was relief of pain and of the accompanying functional disturbances; often, too, there was a gain in weight and an improvement in general wellbeing.

Touche concludes his article with the statement that "it is certain that the effect is not curative, but it is actually palliative." Delbet, on the other hand, states that he has seen no beneficial effects from the use of colloidal selenium injected intravenously. In the discussion on Delbet's paper, Ledoux-Lebard states that he has observed nothing from selenium further than the temporary improvement which is shown by almost all cancer cases on the application of any new therapeutic measure. In one or two instances the claim is made in the literature of an actual cure of malignant growth through the use of selenium. Such for example is the case described by Blumenthal. From the clinical description this might have been a cancer of the tongue, and was judged to have been such in view of the negative Wassermann. No microscopic examination was made. Salvarsan was given. The patient recovered. It is clear that instances of this type cannot be accepted as beyond criticism, and it is safe to say that nothing more convincing in the way of actual cure is offered in the rather voluminous literature on the use of selenium.

Numerous compounds of selenium, some of them claiming to circulate in colloidal form, have been described, and have been put on the market for use in malignant disease. Such are Walker's sulpho-selene, and selenio-vanadium, which has been prepared in the form of an ointment by Schering and

20. Laurent, M., and Bohec, J.: Med. Press and Circular, 1912, xciv, 461.

21. Touche, M.: Bull. et mém. Soc. méd. d. hôp. de Paris, 1913, xxxv, 451.

Glatz. These preparations lay claim to the same palliative effects which have been previously described for colloidal selenium.

Of the other metals in colloidal form, chiefly silver and copper have come into use. Colloidal silver was first recommended for malignant growths by Vogel. It is obtainable on the market in proprietary form under the name of fulmargin, and also as electrargol. Recently Rohdenburg[22] has made a careful study of the effects of colloidal silver in experimental and in human tumors, and finds that they have no value. Colloidal copper has been used in recent times for the same purpose by Gaube du Gers and by others. I have recently examined the effects of colloidal copper on malignant tumors in man, and have been unable to find that it has any therapeutic value. Furthermore, a study of the distribution of the copper in tumors obtained at operation or by necropsy from individuals so treated failed to show that the copper had been deposited therein.

Finally, preparations similar to those used by Werner and by Caspari in animals have also been used in human beings. In these cases also the authors have been able to record palliative effects on the tumor, but in no instance cures.

We have seen that it has been quite impossible to duplicate in human beings the therapeutic technic employed in animal experiments. We have seen further that the use of a modified technic in animal experimentation has never been productive of favorable results even at the hands of enthusiastic adherents. In striking contrast to these conclusions are the observations made in human therapeutics. For every type of preparation described in the preceding paragraphs, the claim has been made practically without exception that it exercises a markedly beneficial effect on malignant disease in the human being. Not only are the subjective symptoms alleviated, but also the tumors appear to become cleaner and softer; the rate of growth is retarded; necrosis and metastasis are prevented, and inoperable tumors become operable. How are we to interpret these observations? How are we to explain the fact that they are the almost invariable accompaniment of the most diverse methods of treatment? I have already quoted the statement of Ledoux-Lebard that every therapeutic novelty appears to exercise a favorable effect on cancer cases. The same fact has been observed in a variety of other diseases, such as locomotor ataxia.

In order to arrive at a safe and reliable estimate as to the value of any new or experimental procedure in cases of

22. Rohdenburg, H.: Jour. Med. Research, 1915, xxvi, p. 331.

cancer, it seems advisable to accept certain definite therapeutic criteria by which the cases are to be judged. In the absence of such a method, alterations in symptoms which are actually of no real value or importance receive undue emphasis. The natural course of the disease is associated with such fluctuations that a sanguine therapeutist can gain some encouragement from even the most hopeless cases. Hence it follows that every mode of treatment has found adherents. The market is flooded with cancer drugs, and cancer charlatans flourish in the most highly educated communities. Unfortunately even well trained, honest and reputable physicians have fallen victims to this fallacy, and have lent their names to the support of modes of treatment which in reality produce no determinable effect on the natural evolution of the disease. It was the desire to combat this unfortunate tendency which led me some time ago to attempt to establish a reliable set of criteria of therapeutic effects in cancer. These were embodied in an article[13] which appeared two years ago, and I may be here permitted to quote them *in extenso:*

CRITERIA OF THERAPEUTIC EFFECTS

In determining the effects of any given mode of treatment on a tumor, a variety of criteria may be relied on. Circulatory changes in the tumor, the relief of pain and the restoration of a secondarily impaired function are certain of the criteria on which stress has been laid by the majority of observers in the past. Important as are these criteria in determining the progress of purely inflammatory processes, it is unquestionable that their value in judging of the effects of therapeutic methods when applied to malignant disease is open to criticism. It is a curious and interesting fact that almost every therapeutic claim made in recent years in connection with cancer has included among its virtues the relief of pain. This is true of vaccination with cancer tissue, of Hodenpyl's method and of many others. In view of this very general effect, not much stress can be laid on this symptom, and it is probably fair to assume that in the great majority of these cases the result is in no small measure psychic. The improvement of function is also largely a subjective phenomenon, and as such requires most careful criticism. Osler relates that he has known a patient with gastric cancer to be relieved of digestive disturbances and to gain 18 pounds in weight as the result simply of the visit of a sanguine consultant who denied the presence of a tumor. Improvement in the ability to chew food, to articulate words or to move a limb are phenomena familiar to those who attempt to treat cases of cancer. The victims of this disease seem to be in a very high degree "suggestible" and impressionable and respond nobly to every therapeutic effort.

Circulatory changes in tumors offer an interesting group of clinical symptoms. The observation has often been made, especially in ulcerated new growths, that treatment is associated with swelling, peripheral hyperemia, and an altered character of the discharge. In spite of the fact that there is no reasonable relationship between this congeries of symptoms and the actual cure of the tumor, they generally receive considerable emphasis and are cited as an indication of the specific local action of the agent employed. It is also true, however, that the growth may continue to advance in spite of their presence. It is of some importance to inquire into the mechanism which produces these circulatory changes and into their clinical interpretation. It is a well-known fact that many drugs, when introduced into the body either by the mouth or through the skin, are excreted not only by the normal channels of elimination, such as the kidney or the intestine, but also from such ulcerated surfaces as may be present on the body. This is easily shown to be true, for example, of certain of the anilin dyes, which, when introduced by way of the veins, produce an intense discoloration of the dressings over ulcers. It is likewise true of certain of the metals, such as arsenic. In order to understand the series of events previously enumerated it is therefore only necessary to assume that the therapeutic agent is excreted from the ulcerated surface of tumors. If an irritant, it will tend to produce hyperemia of the margins of the ulcer, and an increase of the secretions. If an astringent, however, it may produce just the opposite of these effects. Such a result, however striking, is purely accidental, and has no necessary bearing on the growth or destruction of the tumor itself. It constitutes a symptom on which no reliance should be placed.

Excluding from consideration all of these secondary factors, we may conclude that the observation of the size of the tumor itself is the sole criterion on which we can place reliance in judging of the effect of therapeutic measures. This implies, in the first place, that a tumor must be accessible to fairly accurate measurement. Tumors of the uterus, for example, and intra-abdominal growths will only exceptionally fall into this class. In the second place, indirect evidence of a decrease in the size of tumors, such as is afforded by the increased permeability of obstructed passages, as in the case of tumors of the esophagus, pylorus or intestine, must be accepted only with great reserve. Remissions in the obstructive symptoms characteristic of such tumors are a frequent feature of the normal evolution of the clinical history of such growths. The relief of obstruction, however, may be due either to necrosis of the obstructing portions of the tumor, while the remainder continues to grow progressively, or to a relief of the accompanying muscular spasm. Finally, evidence of decrease afforded by the roentgenogram

is not sufficiently exact in most cases to afford ground for so important a conclusion as that at present in question.

Not only must there be unquestionable evidence, however, of the diminution in size of the tumor, but this diminution must be of a kind not ordinarily attributable to the natural evolution of the tumor. . . . It is safe to say that multiple tumors offer enormous difficulties in the matter of interpreting therapeutic results. At present we have in the wards of the hospital a patient with multiple metastatic carcinomas of the skin. For several months we have at intervals made accurate measurements of certain of these tumors and have found that some have undergone retrogression, others have entirely disappeared, while still others have continued to grow steadily. In the case which afforded the ascitic fluid used in Hodenpyl's experiments, many of the lymphatic metastases underwent complete retrogression, while the metastatic process in the liver, as was demonstrated at necropsy, increased progressively, and ultimately almost destroyed that organ. Thus, in multiple carcinosis, the retrogression of individual nodules is no indication that therapeutic intervention has produced an improvement.

I shall not delay to emphasize those variations in the size of solid tumors which accompany hemorrhage and its absorption, edematous swelling, necrosis in the depths, and other familiar factors which clinically simulate, or induce, the softening and the reduction that are so often attributed to therapeutic interference. But it is important to draw attention to a similar feature in that type of superficial epithelioma known as rodent ulcer. These new growths not infrequently advance at one point of the periphery, while they recede at another, and thus cicatrization and contracture may simulate a partial recovery. This effect is due in part to alterations not in the growth itself, but in the accompanying ulcerative process. The secretions from the growths, especially if confined under dressings, may have eroded and destroyed the surrounding skin, and it is tempting to interpret a recession of the associated ulcerative disease as an indication of a favorable effect on the new growth. It is unquestionably this aspect of rodent ulcers which plays so generously into the hands of the numerous nostrum venders for this disease.

In brief, the demonstrable reduction in size of a tumor, of a kind not to be attributed to the natural processes of evolution of that tumor or of its associated lesions, is the one essential feature of effective therapeutic intervention.

When the various methods of treatment which have been discussed in this paper are judged by the standard advocated above, it is apparent that none of them can lay claim to therapeutic effectiveness. The modifications of the disease attributed to them are modifications which occur spontaneously in a very large proportion of cases as a result of the natural evolution of the disease process. This is a fact

which cannot be too strongly emphasized. Owing unfortunately to the hopeless character of cancer, men are not prone to study with care all the lesser changes which the disease and the patient present under ordinary conditions; but when a "cure" is under investigation, the patient and his medical attendant note every apparent improvement with painstaking attention and enthusiasm. As a result, some evidence of improvement in treatment is entered on the books.

970 Park Avenue.

SECRETOGEN

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., May 1, 1915, p. 1518*)

The Council has authorized publication of the following report dealing with two internal secretion specialties—Secretogen Elixir and Secretogen Tablets—to call attention to the unfounded and extravagant claims made for this class of products.

W. A. PUCKNER, Secretary.

Test tube experiments show that pepsin hydrolyzes proteins in acid solutions; that pancreatin digests protein in alkaline liquids, and that diastase converts starch into sugar. Based on these facts, it was assumed that these ferments would aid digestion. This assumption was correct if limited to certain cases of dyspepsia in which it can be shown that certain ferments are absent or deficient. But this limitation was not realized or remembered; on the contrary, the indiscriminate use of digestive ferments in all kinds of cases of indigestion became widespread and still continues, although to a less extent. Herein lies the great disappointment that has followed the use of these ferments.

More recently hormones were discovered, and while their importance has not been fully worked out, it has been assumed that they are responsible for the secretion of digestive ferments, and that in their absence this secretion fails. Without waiting for proof of this assumption, that is, that digestive failure is due to lack of hormones, proprietary medicine promoters are already placing on the market various secretion specialties.

As an example of this new class of specialties and of the unfounded claims made for them, your referee presents the following report on Secretogen Elixir and Secretogen Tablets offered to physicians by the G. W. Carnrick Company.

Secretogen Elixir is said to contain pancreatic secretin obtained from the duodenum with 1/10 of 1 per cent. of hydrochloric acid. Secretogen Tablets are said to be prepared from pure secretin and succus entericus obtained from the epithelial cells of the duodenum. The claims for Secretogen are based on the physiologic action of secretin as described by various observers. To determine whether these claims are justified it becomes necessary to review the evidence advanced to prove that secretin stimulates the digestive glands.

Secretin is a hormone, a chemical substance produced by the action of hydrochloric acid on a previously formed substance, "prosecretin," contained in the cells of the intestinal mucous membrane, especially of the duodenum. Secretin is absorbed by the blood and carried to the pancreas, liver and intestinal mucosa, which are thereby stimulated to produce their characteristic secretions, namely, bile, pancreatic juice and succus entericus. When secretin is injected into the blood, it causes an increase in the flow of these secretions. Some observers have claimed that secretin is absent in cases of diabetes in which the pancreas is still found normal. Wentworth[1] reported several cases of marasmus in which he found no evidence of prosecretin. This deficiency, be believes, is the cause of this disease.

The Carnrick Company, adopting the foregoing views, namely, that secretin is necessary to secure the normal action of pancreas, liver and intestine, as proved, placed on the market their specialty "Secretogen," to take the place of the missing secretin.

The foregoing conclusion cannot, however, be sustained. There are numerous cases in which no hydrochloric acid is produced in the stomach and hence—as it is produced by the action of hydrochloric acid—no secretin can be produced in the intestine. Yet in these cases the pancreatic juice and bile are secreted in normal amounts and digestion goes on normally after the food leaves the stomach. In such cases the pancreas and liver must be stimulated to secretion by some other mechanism than secretin.

The proof that the absence of secretin is characteristic of diabetes or of marasmus is not yet available. Sweet and Pemberton[2] found that many circumstances interfered with the

1. Wentworth, A. H.: The Cause of Infantile Atrophy, Deduced from a Study of Secretin in Normal and Atrophic Infants, THE JOURNAL A. M. A., July 20, 1907, p. 204.

2. Sweet, J. E., and Pemberton, R.: Experimental Observations on Secretin, Arch. Int. Med., February, 1908, p. 231.

extraction of secretin, so that the mere failure to obtain it in a given case is not proof of its absence, unless the various inhibiting influences are given due consideration. The conclusions reached by these authors are that "the evidence so far adduced that secretin is absent in some varieties (of diabetes) does not seem conclusive," and that "the specific absence or deficiency of secretin in marasmus seems to remain as yet unproven."

The favorable reports of Moore[3] in regard to the use of secretin in diabetes are not confirmed by the experience of Foster[4] in five cases, or by the case reported by Dakin and Ransom.[5]

In regard to the use of secretin in intestinal disorders, the G. W. Carnrick Company refers to an article by J. W. Beveridge.[6] An examination of this article shows it to be unscientific and uncritical. The author presents four cases to "demonstrate the peculiar potency exercised by secretin." Of the first he says:

"Stomach was dilated, food delay, seventy-two hours; hyperacidity, vomiting daily, five to twelve times, urine high specific gravity, over 3 per cent. urea, trace albumen."

The patient improved somewhat after gastro-enterostomy with removal of the gallbladder; the vomiting ceased, but the stools continued clay-colored and the high urea output still kept up. Secretin was given, and after this the report continues:

"The stools became normal in color at the end of the second month, weight gradually increased until 122¾ pounds was reached and the urea is now normal, averaging about 1 per cent."

This case is offered to prove the absence of secretin and its effect when given by the mouth. As evidence of hepatic insufficiency the author apparently relies on the color of the stools, and for pancreatic insufficiency he cites the high urea output. He claims that when the pancreas does not furnish an efficient secretion, the proteins of the food fail to be converted into amino-acids, and instead, raise the percentage of urea. Consequently, he concludes that a high percentage of urea indicates the absence of secretin. It is usually held

3. Moore, Edie and Abram: Biochem. Jour., 1906, i, 28; ibid., i, 446.
4. Foster, N. B.: Cases of Diabetes Treated with Secretin, Jour. Biol. Chem., January, 1907.
5. Dakin, H. D., and Ransom, C. C.: Treatment of Case of Diabetes with Secretin, Jour. Biol. Chem., January, 1907.
6. Beveridge, J. Wallace: Secretin, Am. Jour. Gastro-Enterology, April, 1914, p. 170.

that a high percentage of urea depends on two factors, ingestion of a large amount of protein and concentration of the urine. The author gives no data as to the amount of albuminous food, the amount of urine, or whether the percentage of urea was learned by examining a single specimen or the total quantity for twenty-four hours. The mildest judgment that can be passed on such clinical data is that they are totally inadequate. Without doubt the percentage of urea could have been reduced to "normal" by causing the patient to drink water freely. The remaining cases show similar hasty conclusions from insufficient data, rendering them worthless as evidence.

The G. W. Carnrick Company introduces a number of testimonials as to the value of Secretogen. These testimonials are similar to all testimonials. They include no evidence of careful diagnosis, and present an uncritical estimate of the results. They show that the writers have given Secretogen Elixir or Tablets indiscriminately in almost the whole range of digestive disorders, in nephritis, neuralgia, liver disease and gallstones, exophthalmic goiter, neurasthenia, epilepsy, etc. As dependable evidence, these testimonials are not worthy of consideration.

A rational basis for the therapeutic value of Secretogen is lacking for the following reasons:

1. No evidence has been presented that the absence of secretin is a cause of gastro-intestinal diseases. It is usually present, and if not present, as in achylia gastrica, there is evidently some compensating arrangement by which the pancreas is stimulated to perform its regular functions.

2. There is no evidence that secretin in any form is physiologically active when administered by the mouth.

REFERENCES

Fleig, M. C.: Action de la sécrétine, Arch. gén. de méd., lxxx, 24.

Charles, J. R.: Treatment of Diabetes with Secretin, Bristol Med.-Chir. Jour., September, 1906; Med. Press and Circular, Nov. 21, 1906.

Meltzer, S. J.: Animal Experimentation in Relation to our Knowledge of Secretions, Especially in Internal Secretions, THE JOURNAL A. M. A., May 7, 1910, p. 1506.

Wentworth, A. H.: The Cause of Infantile Atrophy, Deduced from A Study of Secretin in Normal and Atrophic Infants, THE JOURNAL A. M. A., July 20, 1907, p. 204.

Bambridge and Beddard: Guy's Hospital Reports, 1907, lxi, 161.

Enriquez and Hallion: Nuevas nociones sobre la digestion. Secretin, Importancia fisiologica y patologica, Transactions of 14th Int. Med. Congress, Madrid, 1904.

Enriquez: La Sécrétine Médication acide duodénale Stimulation de function sécrétiniques chez l'homme., Rev. de thérap. méd.-chir., Paris, 1904, lxxi, 187.

BURNHAM'S SOLUBLE IODINE

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., May 15, 1915, p. 1673*)

The Council has authorized publication of the following report on Burnham's Soluble Iodine.

W. A. PUCKNER, Secretary.

Burnham's Soluble Iodine is offered to the medical profession by the Burnham Soluble Iodine Company, Auburndale, Mass., under the claim that by

> ". . . a new process hitherto unknown to chemistry, . . . Iodine is converted into a soluble article—soluble in water and soluble in gastric secretions and in the tissues."

Beyond this no statement as to the qualitative or quantitative chemical identity of Burnham's Soluble Iodine is furnished; this secrecy, of course, has given the preparation a certain mysterious prestige among unthinking physicians.

Burnham's Soluble Iodine was examined in the Chemical Laboratory of the American Medical Association some six years ago[1] and was found to be an alcoholic solution of free iodin (approximately 3 gm. per hundred c.c.) and combined iodin in the form of iodid (equivalent to about 2 gm. of potassium iodid per hundred c.c.). Thus the total iodin content was somewhat less than half of that of the official Tincture of Iodin (Tr. Iodi), which contains 7 gm. of free iodin and 5 gm. of potassium iodid to each 100 c.c. The official tincture, diluted one-half, therefore, would be essentially equivalent to the Burnham preparation, both being miscible with water. The Burnham Soluble Iodine Company objected to the conclusions drawn from this analysis, but admitted the correctness of the analysis itself.

Any one who gathered his first knowledge of the subject from the Burnham advertising might readily infer that no soluble iodin had been known prior to Burnham's Soluble Iodine. This, of course, is not the case; the method of producing a solution of iodin by the use of an iodid has long been known.

The following statement is not only obviously untrue but also nonsensical:

> "In all the history of iodin medication, covering a period of laboratory research of many years duration, every effort to produce a free iodin, *prior* to the evolution of Burnham's Soluble Iodine, was attended by failure."

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1. For report see THE JOURNAL, March 28, 1908, p. 1055.

The company lays stress on the assumed superiority over the iodids of a preparation containing free iodin. This assumption is based on a fallacy. Those who regard free iodin as superior to combined iodin forget that free iodin taken by the mouth is converted in the intestines, by the action of the alkaline intestinal secretions, into an iodid with a small amount of iodate, while administered intravenously (a procedure that, while advocated by the Burnham concern, is therapeutically indefensible) it enters into combination with the alkaline salts and proteins of the blood. The free iodin in Burnham's Soluble Iodine must act in the system as an iodid, and the whole iodin content, to furnish a correct estimate of the value of the preparation, should be reckoned as an iodid.

Bearing this in mind, then, it is evident that the doses of Burnham's Soluble Iodine recommended by the manufacturers are extremely small. They range from 20 minims (equivalent to 1 grain of potassium iodid) to ½ minim (equivalent to 1/40 grain of potassium iodid). From 5 to 20 minims (equivalent to about ¼ to 1 grain of potassium iodid) is the dosage recommended for syphilis; from "1 to 3 minims [equivalent to from 1/20 to 3/20 grain of potassium iodid] three to six times daily" for typhoid and other intestinal diseases. No wonder the exploiters can say that this nostrum does not irritate the intestines, that it is "non-irritating to the weakest stomach" and that there is an "entire absence of toxic action from maximum doses"! Its alleged freedom from the irritating and untoward effects of ordinary iodids is due, not to any inherent superiority of the preparation, but to the insignificant amount of iodid present.

The preparation is advertised for use in an extremely wide range of diseases, in some of which iodid therapy is recognized as of value, while in others it is generally regarded as either worthless or harmful. Given orally or intravenously (the recklessness of the latter method should again be emphasized) Burnham's Soluble Iodine is claimed to be of:

". . . great utility as an internal antiseptic in tubercular affections . . ."

Since, as previously explained, free iodin, when introduced into the body, enters into chemical combination before it has a chance to permeate the tissues, and since the alkali iodids possess very slight (in fact, for this purpose, negligible) antiseptic powers, it is evident that this claim is unfounded. So, for the same reason, is the claim that "as an intestinal antiseptic," Burnham's Soluble Iodine is:

". . . efficient in Typhoid Fever, Enteritis and other intestinal diseases."

It is recommended in exophthalmic goiter, notwithstanding that this condition is generally recognized as contraindicating the administration of iodids, which excite the action of the thyroid gland, and which therefore must be used with great circumspection. An especially indefensible recommendation is that ½ minim of Burnham's Soluble Iodine (equivalent to 1/40 grain of potassium iodid) be administered every five minutes in "membranous croup"—diphtheria—until relief from dyspnea is obtained. But, of all the extravagant claims made for this preparation, perhaps the following is the most reprehensible:

"In the treatment of Phthisis, in its various forms, clinical evidence clearly indicates that the use of SOLUBLE IODINE affords the most potent method of treatment available. Dose — 2 minims, increasing to 5 minims in four ounces water before meals."

Remove the mystery and tell physicians that a dose of 1/40 or ¼ of a grain of potassium iodid is "the most potent method of treatment available" in tuberculosis and the absurdity becomes self-evident. Nor is this the worst feature of the advice here offered. Iodin, by combining with the fatty acids of tuberculous tissues, promotes their autolysis and consequently their softening and breaking down. The products of this autolysis are carried by the lymphatics to healthy tissues and thus may spread the infection. Therefore the use of iodids in tuberculosis, even in small dosage, should not be undertaken lightly.

It is recommended that Burnham's Soluble Iodine, a semi-secret preparation, exploited by means of extravagant and dangerous therapeutic claims, be held ineligible for admission to New and Nonofficial Remedies, and that this report be published.

VENARSEN

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., May 22, 1915, p. 1780*)

The report which appears below was sent to the Intravenous Products Company for consideration. Having considered the firm's reply, the Council has authorized publication of its report along with the explanation sent by the Intravenous Products Company in reference to the variable composition reported for Venarsen, namely, that "only the first few

experimental ampoules, sent to the doctors for clinical tests, were made without the Mercuric Iodide."

W. A. PUCKNER, Secretary.

This product is prepared by the Intravenous Products Company, Denver. The advertising circulars contain inconsistent statements as to its composition. According to one circular Venarsen is

". . . a comparatively non-toxic organic arsenic compound, 0.6 Gm. representing 247 Mg. (3¾ grains) of metallic arsenic in chemical combination. . . ."

According to another circular Venarsen is

". . . a comparatively non-toxic organic arsenic compound, 0.6 Gm., representing 247 Mg. (3¾ grains) of metallic arsenic and .78 Mg. (3/250 grain) metallic mercury in chemical combination."

Neither one of these statements gives any information as to the actual composition of the product. Inquiry addressed to the manufacturers elicited the reply that:

"Venarsen contains in each 5 c.c. 0.6 Gm. Sodium Dimethyl Arsenate, .0016 grams of Mercuric Iodide, .0048 grams of Sodium Iodide in solution in a suitable vehicle for intravenous administration."

The following report of the examination of Venarsen is submitted by the Association's Chemical Laboratory:

LABORATORY REPORT

Three ampules of Venarsen were examined. The first ampule was labeled

"A comparatively non-toxic organic arsenic compound, representing 247 Mg. (3¾ grs.) of metallic arsenic in chemical combination. 5 c.c. — 0.6 Gm."

Practically the same statement appeared in an advertising circular wrapped around the ampule. The second and third ampules bore labels identical with the first. The circulars differed from that accompanying the first ampule in that the presence of mercury is also announced, thus:

"Venarsen is a comparatively non-toxic organic arsenic compound, 0.6 Gm., representing 247 Mg. (3¾ grains) of metallic arsenic and .78 Mg. ($\frac{3}{250}$ grain) metallic mercury in chemical combination and is so prepared and enhanced as to present the ingredients to the blood in their most acceptable form."

Thus, although the potent elements said to be contained in Venarsen are named, its chemical character (the combination in which the elements occur) is not disclosed.

The ampules contained a transparent, odorless solution, possessing the yellow color of salvarsan solution (an aqueous solution of sodium cacodylate, mercuric iodid and

sodium iodid in the amounts said to be present in Venarsen is colorless). Qualitative tests demonstrated the presence in each of the three ampules of sodium cacodylate (sodium dimethyl arsenate), and the absence of arsenites, arsenates, phosphates, arsanilates (atoxyl, soamin) and arsenphenolamins (salvarsan, neosalvarsan). Titrated with normal hydrochloric acid, using methyl orange as indicator (as outlined in New and Nonofficial Remedies, 1915, p. 40), the three ampules were found to contain the equivalent of respectively, 0.219, 0.253 and 0.216 Gm., or an average of 0.244 Gm. arsenic. (According to statements of the firm each 5 c.c. of Venarsen contains 0.6 Gm. sodium dimethyl arsenate [sodium cacodylate], equivalent to 0.247 Gm. arsenic or 41.66 per cent. Sodium dimethyl arsenate, as described in New and Nonofficial Remedies, contains 3 molecules of water and 35 per cent. arsenic. This indicates that the sodium dimethyl arsenate used in Venarsen contains less water of crystallization than the N. N. R. product).

Neither mercury nor iodid could be found in the first ampule. (The company has since explained that mercury was absent only from the first experimental samples.) The second and third ampules contained iodid and mercury in small amount. The exact quantity was not determined because, on the basis of the mercury content declared, a single accurate mercury estimation would have required the purchase of something like 25 to 100 ampules. As each ampule sells for two dollars, the cost of the material was considered prohibitive.

From the foregoing we conclude that the first ampule examined consisted essentially of a solution containing 0.625 Gm. of sodium cacodylate, N. N. R., while the second and third ampules contained 0.722 Gm. and 0.617 Gm. sodium cacodylate, respectively, and in addition, a mercury compound, probably mercuric iodid, dissolved by sodium iodid.

In other terms, Venarsen as now marketed is a simple solution containing approximately 9 grains of sodium cacodylate, 1/40 grain of mercury "biniodide" and ¾ grain of sodium iodid to each full dose.

In the past the preparation has been in conflict—especially serious because of the potent character of the drug—with Rule 1 (secrecy of composition). The manufacturers have removed this conflict by furnishing a statement of composition; and it is to be expected that they will likewise take steps to remove the manifestly erroneous impression now likely to be gathered from the circulars, namely, that the preparation is rather analogous to salvarsan. These conflicts,

however, call for comment, since physicians have doubtless used the material under misapprehensions.

As to therapeutic claims, the preparation is said to be effective and safe in syphilis; "lower toxicity and greater spirochaetacidal power than other known arsenic compounds" are among the claims. No real evidence for either of these claims is presented. Sodium cacodylate has been tried as an antisyphilitic, but with indifferent success; certainly the results have not been comparable to those of salvarsan. The mercury could conceivably enhance its effect, but the dosage appears too small and the course too short for this influence to be pronounced. Moreover, a careful physician would not give arsenic and mercury in fixed proportions.

The claim of comparative non-toxicity is probable enough from what is known about the cacodylate. No physician should feel "safe," however, when injecting intravenously 0.6 gm. of sodium cacodylate every four to six days. Aside from the grave dangers of intravenous injection in general, the possibility of idiosyncrasies to arsenicals should always be borne in mind.

Finally, Venarsen is claimed to be "indicated" in pellagra, tuberculosis, anemia, etc. No evidence is presented on which to base an opinion as to its efficiency in pellagra. Those who have studied that disease would not be likely to resort to this treatment. In tuberculosis and anemia, there is no sufficient advantage in giving the cacodylate intravenously.

To summarize, Venarsen treatment consists essentially in the intravenous injection of large doses of sodium cacodylate. The other ingredients, as well as the name, merely constitute so much mystification. While the cacodylate probably has some effect on the conditions for which it is advised, there is no evidence that its value even approaches that of salvarsan in syphilis, or that the intravenous use is preferable to the ordinary methods. The dangers are manifest, although they may not be so great as with salvarsan. No justification has been established for its use in tuberculosis and pellagra.

Physicians who wish to try intravenous cacodylate administration should have a full realization of the dangers of such treatment, and in order to avoid further risks, will do well to refrain from combining other drugs with the cacodylate in fixed proportions.

It is recommended that Venarsen be held in conflict with Rule 6 (unwarranted therapeutic claims), Rule 7 (poisonous ingredients not stated on label), Rule 8 (name does not express the chemical composition) and Rule 10 (unscientific combination) and that this report be published.

GRAY'S GLYCERINE TONIC

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., July 10, 1915, p. 189*)

The Council adopted the following report and authorized its publication. W. A. PUCKNER, Secretary.

Gray's Glycerine Tonic Comp. (Purdue Frederick Company, New York) is a mixture said to be made according to a prescription of the late Dr. John P. Gray, superintendent of the state hospital, Utica, New York. As to the composition, the following statement is furnished by the company:

"This preparation is a combination of Glycerine, Sherry Wine, Gentian, Taraxacum and Phosphoric Acid with carminatives."

The label declares the presence of 11 per cent. alcohol, and the dose is given as from two teaspoonfuls to a tablespoonful. A study of the ingredients will show that, aside from the alcohol, the mixture contains but one really active drug, gentian. Essentially, then, "Gray's Glycerine Tonic" is a mixture which, in addition to the narcotic effect of the alcohol, depends on a bitter, gentian, for whatever therapeutic action it may possess.

The bitters, of which gentian is a type, were once credited with many therapeutic virtues which time has shown they do not possess. Pharmacologic research has demonstrated that their utility consists in stimulating the appetite through their action on the taste buds. On this account they were believed also to increase the secretion of the gastric juice by a psychic impression. More recently, however, even this has been questioned—by Carlson, for instance.

These facts are fully understood, presumably, by all physicians. Yet, according to the advertising circular, this "tonic," which, for all practical purposes, is merely a simple bitter, is good for thirty-two diseases ranging from amenorrhea to whooping cough!

The conditions in which Gray's Glycerine Tonic is asserted to be especially efficient are described on the label of the bottle and the outside wrapper, in popular terms, more or less typical of "patent medicine" exploitation, such as "catarrhal conditions," and "stomach derangements." Similar statements are contained in the leaflet accompanying the trade package. For instance:

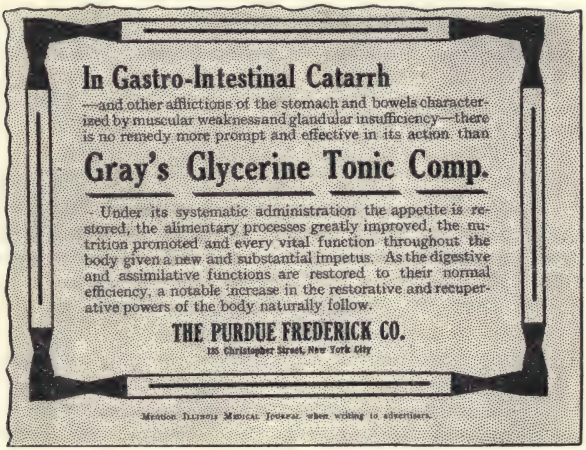
"It is, therefore, an effective, reliable tonic in nervous exhaustion, general debility, impoverished conditions of the blood and nervous system, Bright's disease, diseases of the liver, disorders of the urinary organs, etc."

"It is an unexcelled restorative in that very common class of cases in which there is no positive organic disease, but the patient complains that he 'does not feel well' or 'is out of sorts.' "

Here are some of the claims made in other advertising matter:

"All stages of bronchitis . . . are rapidly improved by the use of Gray's Glycerine Tonic Comp. This remedy has a direct tonic influence upon the circulation of the respiratory mucous membrane; it relieves congestion and restores tone to weakened blood vessels."

". . . improves the appetite, gives valuable aid to the digestive and absorptive processes, and reinforces cellular nutrition in ways that insure a notable gain in vitality and strength."



This appears in a journal owned and controlled by the second largest state medical association of the country.

Even granting that gentian may improve the appetite, how absurd it is to claim that this mixture "relieves congestion," "restores tone to weakened blood vessels," "gives aid to the absorptive processes," "reinforces cellular nutrition," or increases vitality!

Neither the composition of Gray's Glycerine Tonic nor the clinical evidence warrants the belief that it has any therapeutic value other than that due to the psychic effect of the bitter drug gentian. Physicians who have prescribed it have done so because of the advertising. This nostrum has been kept so constantly before the eyes of medical men that they think of Gray's Glycerine Tonic when they cannot remember

the official drugs that may be indicated in the case. The moral is that liberal advertising will sell anything.

It is recommended that Gray's Glycerine Tonic Comp. be declared not eligible for inclusion in New and Nonofficial Remedies on account of conflict with Rules, 1, 6, 8 and 10.

[EDITORIAL NOTE.—An old practice in hospitals—happily now practically obsolete—was to have certain stock mixtures prepared in bulk. Among these there was usually a so-called tonic mixture, used in a more or less haphazard manner when nothing in particular seemed indicated. Such a stock mixture was used in the State Hospital for the Insane at Utica, N. Y., during the many years that Dr. John P. Gray was superintendent (from the early fifties to the early eighties), although it is very doubtful whether he originated the mixture. After the death of Dr. Gray—so the story runs—one of his sons, with a partner, formed the firm of Purdue Frederick Company, and began the exploitation of the elder Dr. Gray's name, in connection, presumably, with this stock preparation. As indicated in the Council's report, Gray's Glycerine Tonic Comp.—and what an absurd name!—is simply a mixture of ordinary drugs, requiring no skill whatever in compounding. If there is a physician living who can not write a prescription offhand as good as this formula, that physician should either go back to a medical school, or change his vocation. There is, and can be, no excuse for prescribing such a ready-made mixture, for every cross-roads drugstore has the ingredients and any pharmacist worthy of the name could compound it. Among the scores of nostrums that disgrace the medical profession of this country, none is more typical of all that is inimical to scientific medicine, to the medical profession and above all to the public—for, after all is said, it is the public that ultimately is humbugged.]

TONGALINE AND PONCA COMPOUND

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., July 17, 1915, p. 269*)

The Council, having considered "Tongaline," "Tongaline Tablets," "Tongaline and Lithia Tablets," "Tongaline and Quinine Tablets" and "Ponca Compound Tablets," found these preparations ineligible for New and Nonofficial Remedies and authorized publication of the following report.

W. A. PUCKNER, Secretary.

TONGALINE

Tongaline (Mellier Drug Co., St. Louis) is a fancy name given to what is essentially a sodium salicylate mixture. The air of mystery created by the name permits the manufacturers to make claims for the product which would be ludicrous if the medical profession was fully conversant with the very ordinary character of the preparation.

Tongaline receives its name from tonga, an inert, long-discarded mixture of various barks and herbs said to be gathered and prepared by Fiji Islanders. Its constituents evidently tend to vary with the collector. The history of the introduction of this indefinite combination of simples is thus given in THE JOURNAL, May 10, 1913.

"A supply of the crude drug was carried to England by a man who had lived for a short time in the Fiji Islands and it was placed in the hands of a retail house in London. This occurred about 1879. In 1880, two English physicians of repute published laudatory articles on the therapeutic value of tonga in neuralgia and rheumatism. This created a demand for the drug which extended to the United States."

Time showed that tonga was inert therapeutically, and authorities on pharmacology now no longer notice it. As the Council previously reported[1] the indefinite character of the mixture should, alone, be sufficient to exclude it from practical therapeutics. During the temporary popularity of tonga, the proprietary mixture Tongaline was put on the market for physicians' use by the Mellier Drug Company, St. Louis. In this, tonga was named as the active ingredient. The commercial interests thus involved have faithfully nourished and kept alive the "tonga" myth.

In a recent advertising booklet "The Therapeutic Properties of the Ingredients of Tongaline," the virtues of tonga, blue cohosh, colchicum, jaborandi and salicylic acid are discussed. The label of a recently purchased bottle reads:

"Tongaline contains Tonga, Cimicifuga Racemosa, Salicylate of Sodium (the salicylic acid being made from pure natural oil) Colchicum and Pilocarpin."

It will be noticed that Tongaline is "made from the pure, natural oil." In fact, the statement is repeated in red ink, in large letters running across the face of the label, thus emphasizing the alleged importance of this assertion. In this connection it is only necessary to recall that it has been proved clinically, chemically and physiologically that there is absolutely no difference between the salicylic acid made from the natural oil and the synthetic.

The formula was thus commented on in the article previously quoted from THE JOURNAL:

"Tongaline . . . is essentially a preparation of sodium salicylate. . . . The Mellier Drug Company realized the impossibility of

1. Reports of the Council on Pharm. and Chem., 1912, p. 40.

creating any marked demand for a nostrum unless it had some real drugs in it—hence the presence of the salicylates. What the actual composition of Tongaline is, no one but the manufacturers know. At one time the following was given as the formula:

Fluid Tonga	30 grains
Extract of Cimicifuga Racemosa	2 grains
Sodium Salicylate	10 grains
Pilocarpin Salicylate	1/100 grain
Colchicin Salicylate	1/500 grain

"These amounts refer to the quantity of drugs in each fluidram of the preparation. Whether the nostrum still has this composition we do not know, but assuming that it has, it is quite evident that sodium salicylate is the essential and active ingredient."

The therapeutic indications given on the label of the bottle are:

"Rheumatism, Neuralgia, Grippe, Gout, Nervous Headache, Sciatica, Lumbago, Malaria, Tonsilitis, Heavy Colds, Excess of Uric Acid, and wherever the use of the Salicylates is indicated."

In a recent booklet this semisecret salicylate mixture is recommended, not only in conditions in which salicylates are indicated, but also combined with aconite for rheumatic fever, with benzoate of soda in the treatment of "grippe," with potassium bromid in nervous headaches, with gelsemium, glycerin and whisky for "heavy colds," with ammonium chlorid, stramonium and cimicifuga in "rheumatic dysmenorrhoea," and even with mercury biniodid as a treatment of syphilitic eruptions!

"When administered with good judgment, Tongaline exerts a stimulating effect upon every organ of elimination; cleansing the complex sewerage system and putting it into working order. When this is done, the sluggish blood current begins to flow more freely; the lymphatic and glandular systems to give up and carry off the toxic products, so long retained . . ."

TONGALINE TABLETS

Then because of a "desire to put Tongaline in a more compact and convenient form," the same concern puts on the market Tongaline Tablets. Whether Tongaline Tablets are of the same composition, the doctor who prescribes them is not advised. In this form we have Tongaline and Lithia Tablets, and Tongaline and Quinin Tablets. Presumably those who are attracted by the word "lithia" are sufficiently uncritical to be content with the statement that:

"The addition of Lithia to Tongaline presents a most useful combination which does not rely upon its action on the kidneys alone as is the case with Lithia salts or Lithia waters as administered . . ."

And the foregoing quotation, be it remembered, is for the information of the medical profession! Tongaline and Lithia Tablets, we are informed, are:

". . . particularly indicated for certain diseases which are caused by deposits of urates in the joints and kidneys, and can be used with much benefit for many people who indulge in generous or intemperate habits of living."

Tongaline and Quinine Tablets are also exploited without statement of composition. The promoters are probably justified in feeling that physicians who prescribe quinin in combination with "Tongaline" care little about the dosage.

It is unnecessary to discuss the silly claims made for Tongaline and its combinations, although it is worth while to point out that the prescribing of such nostrums by physicians is an imposition, if not a fraud, on the public.

PONCA COMPOUND

Ponca Compound, also made by the Mellier Drug Company, St. Louis, is a "female weakness remedy" in tablet form. The name suggests that "ponca" is a medicinal substance, and, in fact at one time, "Ext. Ponca" was named as an ingredient. The nature of "Ext. Ponca" was apparently never explained. It is now replaced in the "formula" by "senecin," and the only information concerning the composition at present given is:

"Ponca Compound Tablets Contain Extract of Mitchella Repens, Senecin, Helonin, Caulophyllin and Viburnin."

This "formula" is practically meaningless, not only because the amount of each ingredient is not stated, but also because "senecin," "helonin," "caulophyllin" and "viburnin" are in themselves variable mixtures of unknown composition.[2]

2. See Report of the Council on Pharmacy and Chemistry on "Resinoids and Concentrations," THE JOURNAL, Nov. 13, 1909, p. 1655.

Presumably, "senecin," "helonin," "caulophyllin" and "viburnin" are extractives of some kind prepared respectively from senecio aureus (life root), helonias dioica (false unicorn), caulophyllum thalictroides (blue cohosh) and viburnum prunifolium or opulus (black haw or cramp bark). These are, one and all, practically inert drugs. There is no reason to believe that any or all of them can have any beneficial influence in the many and varied conditions for which Ponca Compound is advertised.

The following are excerpts from the advertising matter:

"Ponca Compound is a remedy of a very beneficial character for Functional, Uterine and Ovarian troubles, which will respond to internal treatment, especially when digital examination or surgical interference is undesirable."

"Ponca Compound is also valuable during gestation and after parturition."

"Uterine Alterative for Leucorrhoea, Dysmenorrhoea, Amenorrhoea, Metritis, Endo-Metritis, Menorrhagia, Metrorrhagia, Irregular Menstruation, Subinvolution, Painful Pregnancy."

It is recommended that Tongaline and Ponca Compound and all their preparations be held in conflict with Rule 1, in view of their semisecret and indefinite composition; with Rule 6, for the grossly exaggerated therapeutic claims made for them; with Rule 8, because of their misleading names, and with Rule 10, in view of their unscientific character as irrational combinations. It is also recommended that this report be published.

ALFATONE

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., Aug. 7, 1915, p. 548*)

The Council has found Alfatone ineligible for New and Nonofficial Remedies and has authorized publication of the following report. W. A. PUCKNER, Secretary.

Alfalfa is good cattle feed but only nostrum exploiters have suggested its use as a medicine for human beings. While it may seem a waste of time to discuss the medicinal value of alfalfa its recent exploitation by the Norwich Pharmacal Company, Norwich, N. Y., as "a reconstructive tonic and nutrient" in the form of a mixture called "Alfatone," calls for comment. According to the label on the preparation:

"Each fluidounce represents:

Alcohol	15 per cent.
Medicago sativa (Alfalfa)	120 grains
Taraxacum	2½ grains
Gentian	1 grain
Berberine Hydrochloride	1/40 grain
Glycerin and Aromatics."	

"Dose.—One to three fluidrams (4 to 12 c.c.) 4 times daily."

Each maximum dose, therefore, should represent 45 grains of alfalfa, 1 grain of taraxacum (dandelion), ⅜ grain of gentian, 1/100 grain of berberin hydrochlorid, and 27 minims of alcohol. Since the bitter drugs are present in such small amounts that the preparation is almost devoid of bitterness, and as the medicinal value of alfalfa is practically nil, it is evident that whatever action Alfatone may have is due to the stimulant effects of the alcohol.

Some of the claims made for Alfatone are:

"A reconstructive nutritive tonic indicated in general debility, neurasthenia, convalescence, etc."

". . . a Galactagogue of merit as well."

". . . improves the appetite, aids the processes of digestion and assimilation, facilitates elimination and effects gradual but decided gains in strength, vitality and weight."

It is suggested that:

". . . in case of idiosyncrasy the addition of Tr. Nux Vomica 5 to 10 minims to the dose, unless contra-indicated, will secure excellent results."

The Norwich Pharmacal Company naively remarks:

"The dearth of medical literature on Alfalfa has lead us to present below a few of the findings of the Bureau of Plant Industry of the Department of Agriculture . . . as well as those from several state experiment stations . . ."

Here are the "findings":

". . . Digestible nutrients in 100 pounds of Alfalfa, . . . Protein, 11.0 pounds; Carbohydrates, 39.6 pounds; Ether Extract, 1.2 pounds."

". . . The high value of Alfalfa is due to the amount of protein that it contains; to the large percentage of protein that is digestible and to the palatability of Alfalfa."

". . . Table showing pounds of elements removed from the soil by one ton of crop.

	Alfalfa	Wheat
Potash	49.79	12.52
Phosphoric Acid	8.27	9.08
Lime	43.51	2.95
Nitrogen	44.01	22.30"

". . . The abundance of muscle and bone producing material in Alfalfa makes this crop especially good."

Thus estimates of the value of a farm crop and cattle fodder are made to do service as testimonials to its therapeutic merit for human beings! Has the "patent medicine" promoter ever dared to insult the intelligence of his patrons by a cruder absurdity? Yet it is not to the non-technical and unscientific public, but to a profession presumably scientifically trained in pharmacology and therapeutics that this concern presumes to offer its fodder tincture on the basis of testimony to the agricultural value of the fodder plant.

Alfatone is a worthless alcoholic cordial. The audacity of the attempt to promote its sale by a discourse on the merits of a well-known fodder plant is the sole reason for devoting any attention to it. It is recommended that Alfatone be held ineligible for New and Nonofficial Remedies, and that this report be published.

[Editorial Note.—What a comment on American medicine that a concern can even contemplate the possibility of making a commercial success of the sale of such a silly nostrum

as Alfatone! And, yet, when one remembers that a proprietary in which oats constitutes one ingredient ("Pas-Avena") for years has been advertised to physicians and presumably prescribed by them, it is not altogether inexplicable that business men should get the impression that the medical profession is "easy" enough to "fall for" anything in the line of proprietary mixtures. Perhaps we may look forward to being offered proprietaries based on other cheap and well-known fodder plants. Tincture of Timothy Hay, Blue Grass Tonic, Cornhusk Wine! Why not? The enterprising companies that may put them out can easily publish tables to show the digestible nutrients in each and indubitable testimony can be furnished to prove the excellence of any of them as stock feed. If a pitchforkful of timothy hay makes a good fattening ration for a growing steer why should not a teaspoonful of tincture of timothy hay make a "reconstructive tonic and nutrient" dose for a man? If an arm load of thistles (carduus) makes a luscious food for *Equus asinus* why should not a pinch of thistle in alcohol and water be a good "tonic"? Great are the possibilities! They are limited only by the gullibility of the medical profession and the public. Certain it is that some proprietary manufacturers are firmly convinced that no combination can be too preposterous to be worth trying on the medical profession.]

FORMAMINT

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., Aug. 28, 1915, p. 816*)

The following report has been authorized for publication.

W. A. PUCKNER, Secretary.

Formamint is a proprietary medicine manufactured by the A. Wulfing Company (New York, London and Berlin), which is affiliated with the Bauer Chemical Company.

It has been widely advertised in Europe for several years, and is now on the American market;[1] it is advertised in this country both in newspapers and medical journals.

Following is a brief review of the more important alleged investigations that have been reported from time to time in various European journals.

In "The Therapeutical Value of Formamint in Septic Affections of the Oro-Pharynx," De Santi[2] quotes Rosenberg,[3]

1. THE JOURNAL A. M. A., Feb. 24, 1912, p. 572.
2. De Santi: Medical Magazine, 1907, xvi, 141.
3. Rosenberg: Lancet, London, 1905, ii, 1871.

who reports the successful use of Formamint in cases of streptococcus infections, tonsillitis and acute symptoms of chronic sore throat. According to Seifert[4] Formamint is a chemical combination of formaldehyd and milk sugar. When the tablets are dissolved in the saliva, 0.01 per cent. of formaldehyd in its "status nascendi" is liberated and exercises a strong disinfectant action. Seifert states that the preparation is markedly palatable, since it contains a little citric acid to render the taste cool and refreshing. In some experiments with streptococci, pneumococci, typhoid and diphtheria bacilli, Seifert found that a solution of one tablet in 10 c.c. of water destroyed these germs in from five to ten minutes. A solution of the same strength was also added to culture tubes of broth, agar, and gelatin, with the result that no growth occurred in them, while distinct and characteristic development of the bacteria took place in control tubes. He does not state, however, how much Formamint solution was added to the mediums.

Daus[5] reports successful treatment of tonsillitis, mumps and middle ear diseases. In these cases no other gargles or mouth washes were used. He states that no indication of irritant or other injurious action made its appearance even after large doses. In the same article F. Levy reports experiments as follows: Agar plates were prepared with a culture of streptococcus from a severe case of quinsy. One half of the plate was rubbed with saliva containing Formamint in solution. (The strength of the solution used is not given.) In twenty-four hours streaks of growth had appeared on one portion of the plates while the part on which the Formamint saliva had been rubbed remained sterile. Daus also found that agar and broth cultures of streptococcus shaken with Formamint saliva remained sterile.

Rheinboldt,[6] investigating the effects of Formamint and of ordinary formaldehyd on animals, concludes that formaldehyd is toxic in action while Formamint is not.

Rosenberg[7] corroborates this statement. He also found that agar plates of *Bacillus prodigiosus* were killed by Formamint solutions in about four hours. He fails, however, to give the strength of his Formamint solutions.

Wingrave[8] suggests the use of Formamint for infants! He recommends that a tablet be crushed and wrapped in

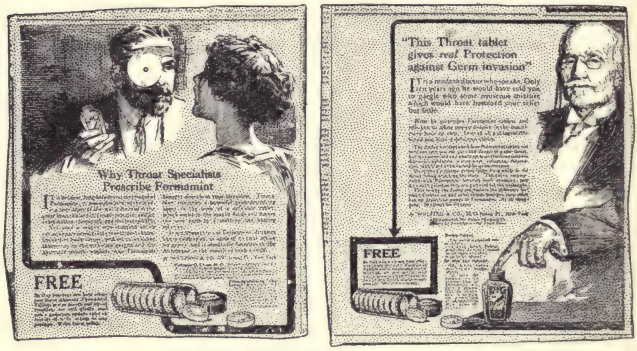
4. Seifert: Pharmakol. u. therap. Rundschau, 1904, No. 14; quoted by De Santi (Note 2).
5. Daus: Med. Klin., 1906, ii, 410.
6. Rheinboldt: Deutsch. med. Wchnschr., 1906, xxxii, 587.
7. Rosenberg: Therap. d. Gegen., 1905, vii, 55.
8. Wingrave: Lancet, London, 1906, ii, 1067.

"butter cloth." The ends of the cloth are to be tied with thread, the Formamint is to be moistened, and the packet is to be held in the mouth of the baby several times each day.

Young[9] published the results of some experiments by himself and Delépine on the human throat. They dissolved a tablet in the mouth and made swab cultures with the following results:

Immediately	after taking the tablet....	0 colonies
10 minutes	after taking the tablet....	35 colonies
30 minutes	after taking the tablet....	150 colonies

They found no staphylococci at any time. Other results of swabbing various parts of the throat before and after the use of Formamint, reported by these investigators, show



How the exploiters of Formamint capitalize the medical profession. Miniature reproductions of typical Formamint advertisements appearing in the newspapers.

enormous reductions in the count, claimed to be due to the action of Formamint. The count was made on agar at 37 C., but they fail to state the time elapsing between taking the Formamint and making the swab. Young also reports favorable clinical results in cases of scarlet fever, diphtheria, sore throat, and the like. It must be noted, however, that they state that the mouth and fauces must first be thoroughly cleansed by swabbing and douching before Formamint is used.

THE "CHEMICAL COMPOUND" CLAIM

The claims made in the advertising literature of Formamint are very extravagant. Many are highly improbable. These statements will be discussed later.

9. Young: Lancet, London, 1908, i, 975.

The statement is made that Formamint is a new chemical compound:

"Formamint is Pentamethanallactose, 5 $CHOH + C_{12} H_{22} O_{11}$. It is an original combination of Formaldehyde with Lactose, a definite chemical compound. The Formaldehyde molecule is locked up in it until solution in the saliva takes place, when the Formaldehyde is liberated in its *nascent* state and is therefore active without being irritant."

Furthermore the makers contend that this new chemical compound is entirely harmless. For example Daus,[5] in an article on "The Disinfectant Action of Formic Aldehyde on Mucous Membranes," declares:

"No indication of irritant or other injurious action made its appearance even after large doses. The urine remained free from albumin and sugar."

Such statements as these are found in the advertising literature:

"Formamint tablets are absolutely harmless and innocuous, even to little children."

"When dissolved in the saliva, Formamint Tablets liberate slowly Nascent Formaldehyde in a most active yet non-irritant form."

They maintain that Formamint is not only absolutely harmless, but actually beneficial to the tissues. It may be used "to tone up and strengthen the tissues, prevent hoarseness, and allay irritation in singers, public speakers," etc.

The claims urged as to its germicidal power are indeed glittering. This "new chemical compound" is claimed to liberate formaldehyd in some new and peculiar condition which, while it has a soothing and tonic effect on the cells of the human tissues, can at the same time quickly kill any form of bacterial life.

"Dissolving readily it releases its germicidal, antiseptic qualities, which impregnate the saliva and are carried naturally and easily around the mouth and in the deepest crevices of the throat — destroying the germs where they are causing the mischief. Formamint prevents and destroys infectious germ life in a soothing grateful way."

"In the saliva it frees a germicide, fatal to germs but harmless to the most delicate membranes. And flowing into every tiny corner of the gums, tonsils and throat, into places where no gargle ever reaches, it most effectively *disinfects* the throat."

The claims as to the preventive and curative effects of the preparation cover a large portion of the category of human ailments and distresses. The following quotations indicate some of its supposed properties:

". . . it is therefore self-evident that Formamint should be looked upon as a necessary part of the treatment of all forms of tonsillitis."

"The value of Formamint is equally great in diphtheric tonsillitis, or as a prophylactic . . ."

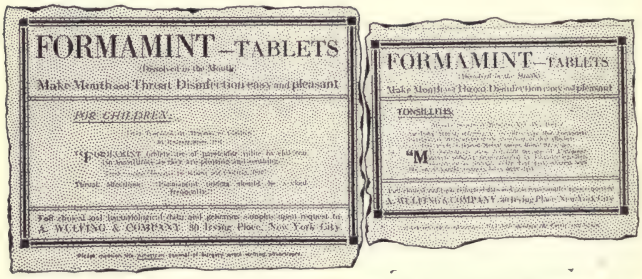
"The extraordinary success which I had with Formamint in a school epidemic of scarlet fever during May and June, 1907, was the determining factor which induced me to abandon the use of inhalations, gargles, local applications in the treatment of diseases of the throat, and to use Formamint exclusively for the future."

"There are naturally many similar conditions in which Formamint may be used as a prophylactic, notably scarlet fever, mumps, streptococcal and staphylococcal sore throats, 'milk outbreaks' of sore throat, drain throats, hospital throats, and the like."

"Formamint Tablets are indicated in Angina, Tonsillitis, Pharyngitis, Stomatitis, Gingivitis, Glossitis, ulceration, spongy or bleeding gums, Pyorrhoea Alveolaris, 'Smoker's Sore Throat,' Abscess or Boils, etc."

"As a *Prophylactic* against Diphtheria, Scarlet Fever, Influenza, Measles, Epidemic Poliomyelitis, and other pathogenic micro-organisms. To neutralize putrefaction products in and about the teeth, correct fermentative processes, deodorize and purify the breath, etc."

"To *tone up,* and *strengthen* the tissues, prevent *hoarseness,* and *allay irritation* in singers, public speakers, neutralize the effects of dust-infection or *disinfect the saliva or sputum* in Influenza, Tuberculosis, etc."



Two Formamint advertisements reproduced in miniature typical of those appearing in a certain type of medical journals.

One man declares that along with specific constitutional treatment he "had the best results from the use of Formamint tablets" in a case of syphilitic ulceration of the tongue.

In short, Formamint is recommended for the treatment or prevention of almost everything, from a bad breath to such grave conditions as scarlet fever, diphtheria and tuberculosis, conditions in which a delay in proper treatment—for instance, in diphtheria, a failure to administer antitoxin—may result in the death of the patient.

A series of investigations was therefore undertaken in order to discover whether the extravagant claims regarding the germicidal power of Formamint could be verified.

Experimental Data

Two fifty-cent bottles of Wulfing's Formamint were purchased in the open market and were kept well stoppered to prevent deterioration.

Qualitative tests showed the presence of formaldehyd and the amount was determined quantitatively by the hydrogen peroxid method as given by Sutton.[10] The results were respectively, 1.99 per cent. and 2.03 per cent. of formaldehyd.

Some determinations were made of the germicidal power of Formamint in vitro, that is, under controlled laboratory conditions. A twenty-four-hour plain agar culture of *Staphylococcus aureus* was washed off in 10 c.c. of sterile 0.85 per cent. sodium chlorid solution. A 1:100,000 dilution of this was made in each of three flasks containing 100 c.c. of sterile saliva. Flask 1 contained 1 per cent. of Formamint, Flask 2, 5 per cent.; Flask 3, containing no Formamint, was kept as a control. At intervals samples were removed

TABLE 1.—SHOWING TIME IN WHICH CULTURES OF STAPHYLOCOCCUS AUREUS WERE KILLED BY DIFFERENT AMOUNTS OF FORMAMINT

Amount of Formamint in Saliva (Per cent.)	Period of Standing at 37 C. (Hours)	Average Count When Plated	Count on Flask of Saliva without Formamint
1	3	32	3200
1	6	0	7000
5	1	Few	5000
5	2	0	4100
5	3	0	3200*
5	6	0	7000*

* The last two observations were made at the same time as on the 1 per cent. solutions.

and dilutions made and plated in duplicate on standard agar. The plates were incubated twenty-four hours at 37 C., and plates containing less than 200 colonies were counted. The results are given in Table 1. After seven days there was no appreciable difference in the plates.

Another test was made by adding a 1 per cent. Formamint solution to plain agar plates inoculated with *B. coli*. A twenty-four-hour plain agar culture of *B. coli* was washed off in 10 c.c. of sterile 0.85 per cent. sodium chlorid solution. A 1:1,000,000 dilution was made of this and 1 c.c. added to each plate. Varying amounts of the 1 per cent. solution of Formamint were added to each plate. They were incubated seventy-two hours at 37 C. After seven days' incubation the count was the same. The results are given in Table 2.

10. Sutton: Volumetric Analysis, Edition 10, p. 390.

Another experiment was made thus: One loopful of a twenty-four-hour plain agar culture of *Streptococcus lacticus* was mixed with a tube of North medium. One loopful from the inoculated tube was mixed with a second tube of North medium. Both tubes were poured into Petri dishes and allowed to cool. One half of each plate was well smeared with a 10 per cent. solution of Formamint in saliva. After twenty-four hours' incubation at 37 C., only a few colonies appeared on the side to which the Formamint had been applied, while the other half was thickly covered with colonies.

This work so far corroborates that reported in the literature quoted by the manufacturers. But the fact that a compound is a germicide when brought into intimate contact with bacteria in a solution or medium in a test tube or flask does not prove that it will be effective when used in the human throat.

THE ALLEGED GERMICIDAL ACTION

An attempt was made to discover whether or not the claims advanced by the manufacturers as to the perfect germicidal action of Formamint in all the nooks and crannies of the mouth and throat could be confirmed.

TABLE 2.—COUNT OF B. COLI CULTURES WITH DIFFERENT AMOUNTS OF FORMAMINT

No. c.c. of 1 per cent. Formamint	0	0.1	0.3	0.5	0.7	1.0	1.5	2.0	3.0
Count	160	33	39	26	15	12	2	0	0

The first step in attacking this problem was to make comparative counts of the number of bacteria in the throat before and after the use of Formamint. The methods employed were as follows: The throat was gargled with 50 c.c. of sterile 0.85 per cent. sodium chlorid solution. In each case the same length of time, as far as possible, was used in the process. The liquid was collected in a sterile flask. The gargling in a series of experiments was begun not less than two hours after a meal. After some preliminary work the following dilutions of the 50 c.c. of salt solution were found sufficient: 1 : 1,000, 1 : 10,000 and 1 : 100,000. Plates were made in duplicate from each dilution and incubated seventy-two hours at 37 C. The counts were made on plates containing less than 200 colonies. Except where otherwise noted standard agar was used. The mediums were always prepared in the same way.

All the work was carried out under conditions as nearly natural as possible. The Formamint was taken according

to the directions accompanying the trade package. Every opportunity was given the Formamint to penetrate all the crypts and recesses about the mouth and throat. The tablet was allowed to dissolve as slowly as possible, the time usually being five to six minutes, and saliva was thoroughly forced around the mouth before being swallowed. Plating was always done immediately after gargling so that no growth could occur in the salt solution. The results are given in Table 3. The numbers are average counts from several plates and calculated to show the number of bacteria washed out by the 50 c.c. of salt solution.

Finally a determination was made of the number of streptococci in the throat before and after the use of Formamint. The throat was gargled in the manner previously described. The streptococcus count was made by the dilution method as given by Heinemann.[11] Culture tubes were used instead of fermentation tubes. One per cent. dextrose broth was the medium employed. One cubic centimeter was added to each of a series of ten tubes for each dilution and the following dilutions were used: 1:10,000, 1:100,000 and 1:1,000,000.

The results given in Table 4 are the average count from a number of dilutions and are reported as the total number washed out by the 50 c.c. of salt solution.

Discussion

The contention that Formamint contains formaldehyd was confirmed by analysis.

The manufacturers also maintain that Formamint is a new, definite chemical compound, consisting of five molecules of formaldehyd and one molecule of lactose, and that when dissolved in the saliva the formaldehyd is liberated in some new and peculiar form, which they call nascent formaldehyd. This new kind of formaldehyd is, according to the advertising literature, especially powerful in its germicidal properties and at the same time has absolutely no irritating or harmful effects.

NOT A CHEMICAL COMPOUND

Thoms,[12] retained as an expert by the German government, decided, after a series of chemical investigations, that Formamint was not a definite chemical compound, but that it was probably a solid solution of formaldehyd in lactose. He proved that when the process of manufacture was carried

11. Heinemann: Laboratory Guide in Bacteriology, p. 86.
12. Thoms: Arb. a. d. Pharm. Inst. d. Universität, Berlin, 1914, xi, 210.

TABLE 3.—SHOWING THAT FORMAMINT DOES NOT GREATLY DECREASE THE NUMBER OF BACTERIA IN THE THROAT

Conditions of Test	Time Since Preceding Test	Amount of Formamint Used	No. Found in Throat Before Use of Formamint	No. Found in Throat After Use of Formamint
Normal	.....	0	15,600,000	.....
Normal	1 hour	0	38,500,000	.....
Normal	1 hour	0	30,500,000	.....
Normal	.....	0	12,500,000	.....
Normal	1 hour	0	14,500,000	.....
	1 hour	0	23,500,000	.....
Tablet dissolved in mouth and throat gargled one hour later	6 days	1 tablet	.....	15,000,000
Throat again gargled two hours after Formamint was used	1 hour	0	.....	10,050,000
Normal	7 days	0	62,000,000	.....
Normal	1 hour	0	72,500,000	.....
Normal	.....	.....	61,000,000	.....
Tablets were taken, one per hour, and throat gargled one hour after last tablet was taken.	2 days	12	.....	39,100,000
Throat was again gargled two hours after taking last tablet	1 hour	0	.....	59,000,000
Normal	5 days	0	35,000,000	.....
Normal	1 hour	0	62,000,000	.....
Normal	1 hour	0	72,000,000	.....
One tablet was taken each half hour for twelve hours consecutively. Throat was gargled one hour after last tablet was taken.	4 days	24 tablets	.....	175,000,000
Throat was again gargled two hours after last tablet was taken	1 hour	0	.....	168,750,000
Normal	3 days	0	129,600,000	.....
Normal	1 hour	0	177,000,000	.....
Normal	1 hour	0	147,000,000	.....
Normal	3 days	0	79,000,000	.....
One tablet was taken immediately after preceding gargle. Throat was again gargled at end of one hour.	1 hour	1	.....	83,200,000
Throat was again gargled two hours after tablet was taken	1 hour	0	.....	134,750,000
Normal conditions except that mouth and teeth were thoroughly washed with soap just before gargling.	19 days	0	32,600,000	.....
Same as above	1 hour	0	33,125,000	.....
Same as above	1 hour	0	40,375,000	.....
Teeth were not washed. Otherwise normal conditions	2 days	0	33,500,000	.....
Same as above	1 hour	0	43,330,000	.....

Same as above	1 hour	0	54,000,000	.....
Same as above	1 hour	0	50,000,000	.....
Same as above	1 hour	0	67,000,000	.....
Mouth and teeth thoroughly washed with soap just before throat was gargled.	2 days	0	5,270,000	.....
Same as above	1 hour	0	10,916,000	.....
Same as above	1 hour	0	8,275,000	.....
Normal conditions, but 1 c.c. of sterile rabbit's blood was added to each plate.	3 days	0	228,750,000	.....
Count from the same gargle as above. No blood used in the plates	0	0	60,625,000	.....
Normal conditions, but count was made on blood agar	1 hour	0	431,250,000	.....
Count from the same gargle as above. No blood used in the plates	0	0	59,625,000	.....
Normal conditions, count was made on blood agar	2 days	0	683,300,000	.....
Same gargle as above, but count was made on plain agar	0	0	58,500,000	.....
One tablet was taken just after preceding gargle. After one hour throat was again gargled. Count on blood agar.	1 hour	1 tablet	.....	558,300,000
Same gargle as above, but count was made on plain agar	0	1 tablet	.....	55,875,000
Normal conditions	2 days	0	79,125,000	.....
One tablet was taken just ten minutes before gargle was made	1 hr. & 16 min.	1 tablet	.....	56,250,000
Normal conditions	2 days	0	46,750,000	.....
One tablet was taken just ten minutes before throat was gargled	1 hour	1 tablet	.....	38,500,000
Teeth and mouth were thoroughly washed with soap just before gargle was made.	5 days	0	47,370,000	.....
Teeth washed as above and one tablet taken ten minutes before gargle was made.	1 hour	1 tablet	.....	21,225,000

TABLE 4.—SHOWING THAT FORMAMINT FAILS TO REDUCE THE NUMBER OF STREPTOCOCCI IN THE THROAT

Conditions of the Test	Time Since the Preceding Test	Amount of Formamint Used	No. Found in Throat Before Use of Formamint	No. Found in Throat After Use of Formamint
Normal	.....	0	1,200,000	.....
One tablet was taken and throat gargled one hour later	4 days	1 tablet	.....	14,750,000
Normal	3 days	0	9,950,000	.....
One tablet was taken and throat gargled ten minutes later	1 hour	1 tablet	.....	8,000,000

out in exactly the way called for by the Formamint patents, compounds containing a greater or less per cent. of formaldehyd could be made while the other properties remained similar to those of Formamint. The composition of the final product depended on the proportion of the components used in the process. Therefore Formamint did not form a safe means of uniform dosage.

As a result of Thoms' work the German courts held that Formamint was not a new chemical compound. Consequently the Formamint patent (Number 189036) was annulled in Berlin, Nov. 29, 1913.

Again the contention that formaldehyd in the nascent or active condition is less poisonous and irritating than in its ordinary form is contrary to what would be expected from the behavior of such compounds. If it were liberated, as claimed, in the "nascent" condition, it would be, for that very reason, not only more active but also more harmful.

As a matter of fact, Formamint did have an irritant effect on the worker who carried out these investigations. When one tablet was taken each hour for twelve consecutive hours, marked irritation of the intestinal tract resulted. There was almost sufficient nausea to cause vomiting and uneasiness in the alimentary canal following the experiment. When the twenty-four tablets were taken the results were similar but more pronounced. This is decidedly in contradiction to the assertions of the manufacturers.

Otto Seifert,[13] moreover, cites the following:

"By Effects: Only a few patients complain of an unpleasant sharp taste, burning of the tongue (Seifert, Sklarek). Among the general symptoms observed are urticaria-like exanthems (Glaser, Roters), which are accompanied by nausea, vomiting, headache, insomnia and vertigo, burning and irritability especially in the larynx (Meissner); phenomena of poisoning (Geissler); gastric disturbances (Engelmann); renal irritation (Steinhard); unsuited for diabetics (Voit)."

The contention that Formamint, when mixed directly with mediums and left in contact with bacteria, will kill the organisms was corroborated. Thus the statements and pictures in the booklet, "The Gospel of Prevention," which is enclosed with each bottle of Formamint, showing the inhibition of growth of air bacteria on plates containing Formamint are no doubt true and authentic.

Finally, the claim that Formamint is an almost perfect throat disinfectant was by no means confirmed, as a glance at the tables will show. One hour after it is taken, even when a tablet was used each half hour for twelve hours, the

13. Seifert, Otto: Die Nebenwirkungen der modernen Arzneimittel. 1915.

number of bacteria in the throat was practically the same as when Formamint was not used. Even ten minutes after taking a tablet the number of bacteria in the throat was never greatly reduced as is maintained by the manufacturers.

HAS NO SELECTIVE ACTION

Formamint exerts no selective action in killing off the very delicate organisms which are more apt to be pathogenic. When the comparative counts were made on blood agar which would favor the growth of the delicate parasitic organisms, no reduction whatever was shown by the use of Formamint.

The number of streptococci was found to be the same, within limits of experimental error, ten minutes after taking a tablet as it was before the tablet was taken.

Therefore it seems that Formamint fails, as any such germicide would be expected to fail, to kill bacteria in the crypts and recesses of the throat, for when dissolved in the mouth it cannot reach and remain in contact with the organisms long enough to kill them before it is swallowed.

SUMMARY

Summed up the investigation shows:

1. That the claims made for Formamint are extravagant and misleading.

2. That the recommendations for the use of these tablets may be, in some cases, fraught with danger and are a menace, not only to the health of the individual, but also to the safety of the community.

3. That the claim that Formamint is a definite chemical compound is false.

4. That the use of Formamint may produce marked irritation of the intestinal tract.

5. That Formamint is not a throat disinfectant as the manufacturers maintain, but its action on the bacteria of the throat is an almost negligible one and dependence on Formamint for the prevention of infection and for curing disease is not only unwise but dangerous.

6. That Formamint conflicts with the rules of the Council. False statements are made with regard to its composition (Rule 1); grossly unwarranted claims are made for its therapeutic properties (Rule 6), and therefore its exploitation to the public (Rules 3 and 4) is a public danger.

It is recommended that this report be published, to call attention not only to the falsity of the claims made for, and the danger in the use of, Formamint, but also to emphasize the utter inefficiency of all such methods of "disinfecting" the throat.

IODUM-MILLER AND IOD-IZD-OIL (MILLER'S)

Report of the Council on Pharmacy and Chemistry

(An abstract of this report appeared in The Journal A. M. A., Oct. 2, 1915, p. 1202)

The Council adopted the following report and authorized its publication.

W. A. PUCKNER, Secretary.

A referee has submitted to the Council the following report of the Chemical Laboratory of the American Medical Association on Iodum-Miller and Iod-Izd-Oil (Miller's) (Iodum-Miller Co., Kansas City, Mo.):

The unsatisfactory statements made in regard to the composition of Iodum-Miller and the far-reaching therapeutic recommendations for it induced the laboratory to make a chemical examination of the preparation. It claimed more or less directly that the preparation is entirely new and possesses novel characteristics.

It is asserted that

"Iodum-Miller is made from Soot Iodine, which is our own product. This Soot Iodine is SOLUBLE IN WATER before being combined with its base C.P. Glycerine."

No information regarding "soot iodine" is offered and an inquiry sent to the proprietors by a physician brought only the non-committal reply that "soot iodine"

"is made from Resublime [resublimed?] Iodine by a chemical process which renders it soluble in water before being combined with its base."

Iodum-Miller is said to contain

"Active Free Iodine 2.2 grams per 100 c.c., 10. grains per fluid ounce, 1.7% by weight."

"In addition to the active free iodine . . . IODUM-MILLER carries a still greater per cent of Iodine in its basic combination . . ."

According to the label, the preparation is

"An Iodine for External and Internal use . . . 45 drops equals 1 dr. by weight. Each drop equals the per cent. of iodine in 1 gr. potas. iodide."

Iodum-Miller is a heavy, dark liquid having an odor characteristic of ether (ethyl oxid). Qualitative tests revealed the presence of glycerin, free iodin, iodid and potassium. The specific gravity at 25 degrees was 1.284. Direct titration with sodium thiosulphate solution indicated the presence of 1.68 per cent. of free iodin. A determination of the total iodin content by the Hunter method indicated 3.06 per cent. Subtraction of the amount of free iodin found from the total amount of iodin present, gives 1.38 per cent. combined iodin. Assuming this to be present as potassium iodid, as appears probable from the qualitative examination and from the quantitative determination of potassium, 1.80 per cent. potassium iodid is indicated. From this examination it is concluded that Iodum-Miller is, essentially, a solution of iodin and potassium iodid in glycerin, containing 1.68 per cent. free iodin and 1.80 per cent. potassium iodid. The examination contradicts the assumption that Iodum-Miller is either novel in principle or new. Moreover, accepting the firm's statement that 45 drops weigh 1 dram (60 grains) the examination shows that one drop equals, not "the per cent. of iodine in 1 gr. potas. iodide" but instead, the per cent. of iodin in only 1/20 grain potassium iodid. As the statement that "Each drop equals the per cent. of iodine in 1 gr. potas. iodide" appears on the label of the trade package, Iodum-Miller would seem to be misbranded under the federal Food and Drugs Act.

The recommended internal dosage of Iodum-Miller (from ½ to 20 drops) is equivalent to from 1/40 to 1 grain of potassium iodid. Its external efficacy in comparison with that of other iodin preparations may be estimated by comparing the respective free iodin contents, since the germicidal power of combined iodid is negligible. While Iodum-Miller contains 2.15 gm. free iodin in 100 c.c., tincture of iodin contains 7 gm. per 100 c.c. and compound solution of iodin (Lugol's solution) contains 5 gm. free iodin in 100 gm.

Among the advertising literature is a circular which purports to be a "Certificate from Kansas City Testing Laboratory, By Roy Cross, Secretary." The "certificate" attempts to prove that Iodum-Miller is vastly superior to the official tincture of iodin as a germicide, asserting that "In the process of dissolving [tincture of iodin] in water, a very large amount of the iodin is lost by precipitation. . . ." This is not true of the tincture of iodin which is now official, though it is true of the tincture official in former editions of the Pharmacopoeia. The report ignores completely the widely used aqueous solution of iodin.

Iod-Izd-Oil (Miller's) is said to be an "Iodine Combination" made "from the same Soluble Soot Iodine as is IODUM-MILLER." It is said to "liberate Free Soluble

Iodine" when applied to the skin, mucous surfaces, etc. It is further defined as "Soluble Iodine combined with water-white Hydrocarbon Oil" and is said to liberate "Soluble Iodine 2 per cent." While these statements suggest that Iod-Izd-Oil (Miller's) contains the iodin-potassium iodid combination contained in Iodum-Miller, analysis indicated the oil to be a simple solution of iodin in liquid petrolatum. Quantitative determinations indicated, not 2 per cent. of iodin, as claimed, but only 0.42 per cent. and all of this was present as free iodin.

REFEREE'S REPORT

The following therapeutic claims appear on the label of a bottle of Iodum-Miller:

"EXTERNAL INDICATIONS

"Tuberculosis, Pneumonia, Pleurisy, Cough, Sore Throat, Pyorrhea, Tonsilitis, Rheumatism, Spinal Irritation, Boils, Felons or any Pain. Periostitis, Carbuncles, Fistula in Ano, Goiter, Blood Poison, Diseases of Uterus and appendages (apply full strength on cotton wrapped applicator), Gonorrhea, acute or chronic in both sexes, Orchitis, Bubo, Prostatitis, Swellings, Enlarged Glands, Etc."

"INTERNAL INDICATIONS

"Pneumonia, Tuberculosis, Pleurisy, Typhoid Fever, Syphilis, Catarrh of Mucous surface of Alimentary Canal, Autotoxemia, Vomiting of Pregnancy, Rheumatism, Chronic Glandular and Organic Affections."

The "certificate" from the Kansas City Testing Laboratory, mentioned above, states that Iodum-Miller was found to have a germicidal value nineteen times greater than carbolic acid—a somewhat remarkable finding in view of the fact that iodin dissolved by means of potassium iodid in alcohol or water, when tried on the typhoid bacillus has recently been found to possess only four times the germicidal value of carbolic acid in a solution of the same strength (Maben and White: *Chem. and Drug.*, Jan. 30, 1915, p. 144). The "certificate" further states that the test "shows available iodine as found in IODUM-MILLER to have the greatest bactericidal power of any substance that we have ever tested that can be used medicinally." There is no reason to believe that the desire to please its patrons has led the "testing laboratory" astray from the literal truth. The laboratory's experience may be limited and the statement therefore entirely correct as far as it goes. No mention, however, is made of any tests comparing the germ-destroying power of Iodum-Miller with that of tincture of iodin, which contains 7 per cent. free iodin, unless the casual statement that "Iodum-Miller sterilized [the skin] more quickly" than tincture of iodin, be taken to imply such

tests. It is not clear, however, by what means the laboratory was able to determine that there were no bacteria left alive in the skin after application of tincture of iodin and Iodum-Miller; no details are given of the methods used in arriving at this conclusion.

A circular says that Iodum-Miller

". . . gives the Greatest Bactericidal and Therapeutic Action, whether used Internally, Externally, Hypodermically or Intravenously."

In the light of the preceding report of the Chemical Laboratory of the Association, these claims require little comment. The laboratory has shown that the free iodin content (and consequently the germicidal efficiency) of Iodum-Miller is less than half that of Lugol's solution, and less than a third of that of the official tincture of iodin. As for the advice to use Iodum-Miller internally in diseases ranging from pneumonia to syphilis and from typhoid to tuberculosis, in order to be convinced of its dangerous character, it is necessary only to recall that this treatment is equivalent to the administration of small doses of iodid—from 1/40 to 1 grain of potassium iodid. The mystery being removed from the composition of Iodum-Miller, the absurd extravagance of the claims made for it becomes manifest. The criticisms of the Council on the recommendations for Burnham's Soluble Iodine (THE JOURNAL A. M. A., May 15, 1915, p. 1673) apply in almost every particular to Iodum-Miller.

Unwarranted therapeutic claims are made for Iodum-Miller; incorrect statements are made with regard to its composition and that of Iod-Izd-Oil (Miller's); and the application of a trade name to both of these products is unjustifiable, since neither is original. It is therefore recommended that Iodum-Miller and Iod-Izd-Oil (Miller's) be held ineligible for New and Nonofficial Remedies.

LACTOPEPTINE AND ELIXIR LACTOPEPTINE

Report of the Council on Pharmacy and Chemistry

(From The Journal A. M. A., Oct. 23, 1915, p. 1477)

Mixtures of pepsin and pancreatin are therapeutically irrational; the two substances are not indicated in the same conditions, nor can they act together. Under physiologic conditions, such mixtures are chemically impossible: in a liquid medium the ingredients destroy each other.

Lactopeptine is manufactured by the New York Pharmacal Association, Yonkers, N. Y. It is sold under the claim that it

contains pepsin, diastase, pancreatin, lactic acid and hydrochloric acid. This product was among the first proprietary preparations examined by the Council on Pharmacy and Chemistry. The report of the investigation was published in THE JOURNAL, March 16, 1907, p. 959. The preparation was found to be practically inert—"essentially a weak saccharated pepsin," devoid of tryptic activity.

Six years later it was still widely advertised with the same irrational claims. A referee (A) therefore examined Lactopeptine (powdered) for the Council in 1913, and confirmed the previous findings. The referee's report was published in THE JOURNAL, Aug. 2, 1913, p. 358.

Nearly four months after this publication, the manufacturers protested against the report, maintaining, contrary to the findings of the Council, that Lactopeptine possesses pancreatic activity and contains "loosely combined" hydrochloric acid. Referee A therefore repeated his examination, and a second referee (B), independently, examined specimens of Lactopeptine (powder) purchased on the open market for the purpose shortly before.

A few specimens examined by these two referees showed a slight tryptic activity; most of them showed none. The amount of hydrochloric acid present was insignificant.

The reports of the two referees were referred to the manufacturers, who again protested vehemently against these findings, this time on the ground that the specimens were old. The manufacturers also cited the work of three chemists to disprove the findings of the referees, and demanded that the Council reexamine Lactopeptine, making use of fresh specimens. The Council refused for the following reasons:

1. So long as the packages of Lactopeptine are not dated, the activity of specimens known to be fresh is of no practical importance. The activity of the actual market supply is the only question of interest to the profession. The only fair test is that made on specimens representative of the product sold to the ultimate consumer.

2. The evidence presented by the manufacturers did not warrant a reexamination, since the work of two of the chemists cited substantially corroborates the results obtained by the Council's referees from the fresher specimens. The figures for tryptic activity obtained by the third chemist cited by the manufacturers could not be accepted by the Council, since it was at variance with all other known results of investigations of Lactopeptine.

3. As stated at the outset, whatever the tryptic activity of the mixture, it is therapeutically useless. A demonstra-

tion of tryptic activity in a mixture containing both pepsin and pancreatin is of merely theoretical interest.

Such activity, of course, cannot be expected, even on theoretical grounds, in liquid mixtures like Elixir Lactopeptine.

The Council therefore again declared Lactopeptine (powder and tablets) and Elixir Lactopeptine ineligible for New and Nonofficial Remedies and authorized publication of the following statement.

W. A. PUCKNER, Secretary.

THE COUNCIL'S REPORT*

* Owing to lack of space, the referee's reports are here omitted. They will be given in full in the Annual Reports of the Council.

Lactopeptine powder (New York Pharmacal Association, Yonkers, N. Y.) was examined by the Council in 1907. At that time it was claimed to contain

". . . the five active agents of digestion—pepsin, diastase (veg. ptyalin), pancreatin, lactic acid and hydrochloric acid—combined in the proper proportion to insure the best results."

The examination showed that the preparation was essentially "a weak saccharated pepsin," containing but small amounts of pepsin, no hydrochloric acid, or mere traces only, and no diastase or pancreatin (THE JOURNAL, March 16, 1907).

In 1913, the product was reexamined, because the claims, as to both composition and therapeutic value, were still being made. Samples were tested both of the American product, and of a British product from John Morgan Richards and Sons, London. The original findings were confirmed and the results were published in THE JOURNAL, Aug. 2, 1913, p. 358. Nearly four months later (November 24) the New York Pharmacal Association wrote to the Council, objecting to the findings and maintaining that Lactopeptine possesses pancreatic activity and contains ("in loose chemical combination") hydrochloric acid. In accordance with the custom of the Council, the work was sent back for review to the referee (A), whose conclusions were then tested by a second referee (B), a physiologic chemist, not a member of the Council, selected because of his special knowledge of the subject.

In December, 1913, Referee A made a large number of new tests to determine proteolytic and amylolytic power. His results show that the ferment activity of the preparation is so low as to merit no recognition in practical use. The tests also show that the amount of lactic acid or "loosely combined HCl" (or both) present is too small to have any appre-

ciable physiologic activity and therefore to be of any therapeutic value.

Nine samples of Lactopeptine purchased in the open market in December, 1913, and January, 1914, were examined be Referee B early in 1914. His studies show absence of amylase in all samples; presence of pepsin, giving weak reactions even when compared with those of old pepsin preparations; complete absence of trypsin in seven out of nine samples, tryptic reaction being obtained in two samples, in one of which the reaction, "slight at best and of no practical import," was obtained only after treatment for twelve hours or more.

The presence of tryptic activity in two out of the nine samples may be due to the fresher condition of these specimens, as indicated by the serial numbers. The evidence shows that it is a commercial impossibility to market mixtures of pepsin, pancreatin and lactic acid so that they can display any material tryptic activity.

It should be reaffirmed that mixtures combining peptic and pancreatic activities are not feasible, because pepsin cannot act except in the presence of acid, and pancreatin is destroyed by acid and by peptic activity. Furthermore, in conditions in which pancreatin is called for, pepsin is not, and vice versa; therefore the administration of mixtures of pepsin and pancreatin would be unjustified, even if both constituents could be expected to exert activity.

The foregoing observations apply to Lactopeptine in powder and tablet form.

While mixtures of pepsin and pancreatin are unscientific and unjustified, theoretically the two substances may coexist in a solid preparation, and the activity of such a preparation is consequently a proper subject of investigation. Theoretically as well as practically, however, pepsin and pancreatin cannot exist together in solution. The claims made for Elixir Lactopeptine and all other liquid preparations sold as mixtures of pepsin and pancreatin are therefore impossible. The Council has previously taken action (THE JOURNAL, Feb. 2, 1907, p. 434) refusing to approve for inclusion with New and Nonofficial Remedies such preparations, calling the attention of the medical profession and of manufacturers to their worthlessness, and requesting the American Pharmaceutical Association to instruct its committee on the National Formulary to omit from the next edition of that work a liquid preparation of pepsin and pancreatin recognized under the title of "elixir digestivum compositum."

It is recommended that the Council reaffirm this previous action, and that Lactopeptine and Elixir Lactopeptine be declared ineligible for New and Nonofficial Remedies because of conflict with Rule 10 ("No article will be admitted which, because of its unscientific composition, is useless or inimical to the best interests of the public or of the medical profession").

Manufacturers' Protest and Council's Answer

The foregoing was submitted, together with the findings of the two referees, to the manufacturers. They protested again, alleging that:

AGE OF SPECIMENS

First.—The specimens of Lactopeptine examined by the second referee were old. The dates of manufacture corresponding to the several batch numbers are supplied by the manufacturers as follows:

2275 (Powder)	September, 1908
2301 (Powder)	June, 1909
2312 (Powder)	December, 1909
2348 (Powder)	October, 1911
2352 (Powder)	December, 1911
2364 (Powder)	July, 1912
2374 (Powder)	March, 1913
2383 (Powder)	October, 1913
1638 (Tablets)	October, 1911

The manufacturers assert that they do not understand how specimens of these ages could have been purchased on the open market in 1913 and 1914, inasmuch as their agents are and long have been instructed to take up from the druggist all lots of Lactopeptine which, as indicated by the batch numbers, have attained "any appreciable age." The age of the specimens, the manufacturers declare, deprives the table in the second referee's report of "all significance or interest."

As previously stated, however, the specimens of Lactopeptine examined were purchased on the open market in various localities in unbroken packages, in December, 1913, and January, 1914. They thus represent stock used in filling physicians' prescriptions or sold to the public. Neither the referees nor any one connected with the Council had any means of knowing the age of the specimens until the dates of manufacture were furnished by the New York Pharmacal Association. The first tests of the second referee were made in February, 1914, on Specimens 2374 and 2383, which were then, it would appear, about one year old and four months old, respectively. The Council has repeatedly urged that

pharmaceutical substances which are subject to deterioration should be dated by the manufacturer, and a similar suggestion has been made by the Bureau of Chemistry of the U. S. Department of Agriculture concerning mixtures containing enzymes. Nothwithstanding the instructions which the New York Pharmacal Association claims to have given its agents, the market supply of Lactopeptine in December, 1913, and January, 1914, was not composed of new stock, and until the manufacturers adopt the practice of dating packages, there can be no assurance that it will be fresh. In this connection it is of interest to note that the Bureau of Chemistry of the U. S. Department of Agriculture has issued a warning that it will judge such products by the degree of their activity when they reach the consumer, i. e., as they are found on the market.

REPORTS OF OTHER CHEMISTS

Second.—The New York Pharmacal Association cites the work of several chemists, who have examined Lactopeptine and report the presence of tryptic activity. Dr. S. R. Benedict in December, 1913, reported to the Council "distinct" tryptic activity (digestion in twelve hours by Lactopeptine of 4.2 times its weight of fibrin containing 50 per cent. moisture) in specimens examined by him. These specimens were numbered 2382, and were therefore probably manufactured in October, 1913; compare the dates furnished by the manufacturer for the specimens used by the second referee. No tests against other preparations possessing tryptic activity are reported, and Dr. Benedict expressly disclaims any opinion as to the therapeutic value of the preparation.[1] Dr. P. B. Hawk,

1. Dr. Benedict's personal communication to a member of the Council is as follows:

"In the report of the Council upon Lactopeptine which you sent to me, I find the following statement: 'Careful examination failed to show the presence of either diastase or pancreatin.' In this connection I will cite to you the following experiment, carried out by myself: A package containing a 1-ounce bottle of Lactopeptine (powder) with seal unbroken was purchased in the open market and opened in this laboratory. The label bore the special Number 6 2382. Two hundred milligrams of this product was dissolved in 50 c.c. of a 0.25 per cent. solution of sodium carbonate in water. This solution was divided into two portions of 25 c.c. each. One of these portions was boiled at once, and after cooling was added to 1 gm. of moist fibrin contained in a flask. The other portion (unboiled) was also added to 1 gm. of moist fibrin contained in a flask. Both flasks (after addition of 5 c.c. of toluene to each) were stoppered and placed in an incubator at 37 degrees, and left there for twelve hours. Examination of the two flasks at the end of this period showed that the one to which the unboiled solution of Lactopeptine [powder] had been added contained much less solid protein than did the other. Although this fact was obvious to the naked eye, the exact extent of digestion in the two flasks was determined by heating both to boiling, acidifying with acetic acid, diluting to definite volume, filtering and determining the nitrogen in the filtrate by Kjeldahl's

whose report was submitted by the manufacturers, found in Lactopeptine by Fermi's method one-fifth tryptic activity of that of Merck's pancreatin, and by Grützner's method an activitl of 18 per cent. of the pancreatin. A test for the production of tryptophan was reported positive. The New York Pharmacal Association also submitted a report from Dr. A. W. Balch, who found pepsin, rennin, trypsin, steapsin, amylopsin and lactic acid present in Lactopeptine; also an amount of combined hydrochloric acid in 1 gm. the equivalent of 1.05 c.c. tenth normal solution or 0.00383 gm. hydrochloric acid. (He reports digestion in twenty-four hours by Lactopeptine of 25 times its own weight of fibrin. "An active extract of pancreas reacted exactly like the Lactopeptine solution.") The serial numbers of the specimens tested by Hawk and Balch are not given, but no doubt they were fresh.

CONCLUSIONS

The New York Pharmacal Association demanded that the referee reexamine Lactopeptine, making use of fresh specimens. The Council held that this was unnecessary, for the following reasons:

1. The previous finding of the Council, that specimens of Lactopeptine found on the open market are essentially weak saccharated pepsins, is not to be refuted by examination of fresh specimens. Even if it be assumed that all old specimens of Lactopeptine have been withdrawn from the market since the last purchase of specimens for the use of the Council's referee, there can be no assurance that the stock will be constantly kept fresh. Unless the manufacturers

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method. Subtracting the trace of nitrogen contained in the filtrate of the control flask, the results showed that 42 per cent. of the original fibrin present had been dissolved by the unboiled Lactopeptine solution. This can be ascribed only to tryptic activity under the conditions of this experiment. Furthermore, this is not simply a 'trace' of activity, but is at least sufficiently marked to warrant a statement that this sample showed a distinct tryptic activity. Inasmuch as I have obtained exactly similar results with two other samples of Lactopeptine (powder) (these being the only ones I have examined), I am inclined to question the correctness of the Council's statement regarding the absence of trypsin from this preparation. [As noted above, a fresh preparation was used.—Ed.]

"May I again add that I am making no statement regarding therapeutic value of preparation, and that I have no opinion upon that matter one way or the other. My work was undertaken solely out of interest to see whether trypsin could exist in the powder (which gives a markedly acid solution when dissolved in water). The Elixir Lactopeptine could theoretically show no tryptic activity, nor have I found any trace of such activity in one sample of the Elixir examined.

"In making use of any of the contents of my letters kindly include the statement that my work upon Lactopeptine was done without remuneration of any kind, and was done only for the scientific interest attached to the question."

date their product, physicians cannot know that their prescriptions are filled with fresh material. Nor is it reasonable to ask that the Council examine the market supply of any given proprietary at a time selected by the manufacturers.

2. Without entering into all questions of detail in the analyses, the Council is willing to accept the reports of Drs. Benedict and Hawk as representative of fresh Lactopeptine powder. It is therefore unnecessary for the Council to make further experiments along this line. The results of these two chemists in no wise contradict the conclusions of the Council's referees, being comparable with those obtained by the referee on the fresher specimens used by them. The experiments of Drs. Hawk and Benedict show a degree of tryptic activity which, though chemically not negligible, is quite without significance practically, even if it could be assumed that the trypsin in the fresh Lactopeptine escaped destruction in the stomach. The figures for tryptic activity given by Dr. Benedict do not differ materially from those of the first referee. Those of Professor Hawk show a tryptic activity of from 18 to 20 per cent. of that of commercial pancreatin—and commercial pancreatins ordinarily are of low tryptic activity, if not inert (see Long and Muhleman: *Arch. Int. Med.*, February, 1914, p. 314.) The reports of these chemists present no reason for changing the conclusion that "it is a commercial impossibility to market mixtures of pepsin, pancreatin and lactic acid so that they can display any material tryptic activity."

The results which Dr. Balch obtained in a test for tryptic activity show a marked discrepancy with those obtained by Drs. Hawk and Benedict, not to mention the Council's referees, and also with the fact that only about 11 per cent. of "pancreatin" is claimed in the published formula of Lactopeptine. The Council is unable to accept Dr. Balch's results for trypsin or rennin as reliable. His other results are without significance and call for no special comment.

3. Even if tryptic activity were conceded to Lactopeptine, the preparation, like all preparations containing pepsin and pancreatin, would still be, as previously stated, therapeutically irrational.

The Council approved the report.

Report of Referee A

In view of the manufacturer's reiteration of the claims for Lactopeptine powder, I have carried out further experiments to determine its proteolytic and amylolytic power.

For the proteolytic test I used fresh, well washed fibrin and examined samples of Lactopeptine powder numbered as follows:

No. 1. A part of the English product examined and reported on last spring.

No. 2. A fresh bottle obtained at a Chicago retail drug store in December 1913.

No. 3. A fresh bottle obtained at a Chicago retail store in December 1913.

Portions of 1 gm. each of these samples were mixed with 5 gm. fibrin, 100 mg. of sodium carbonate and 50 c.c. of water in flasks. A little toluene was added to each flask which was then closed with a tuft of cotton and the mixtures were incubated at 40 degrees through twenty-four hours. At the end of that time there was no marked change in the quantity of the fibrin remaining in each flask, the larger part by far being undigested.

As a control I used a sample of an active commercial trypsin, of which I added 500 mg. to the same quantity of water, fibrin and sodium carbonate. This was digested in the same bath at the same time. The digestion was practically completed in less than ten minutes, only minute flakes of the fibrin remaining.

It is evident that the digestive power of the Lactopeptine must be extremely low, and only a small fraction of that exhibited by a commercially good trypsin.

In an experiment with the English sample carried out through nineteen hours as above, using 2 gm. of fibrin and 100 mg. of ferment, it was found by nitrogen tests on the filtrate that about 12.2 per cent. of the protein had been brought into solution, an amount which is practically without importance in a digestion of such duration.

To test the starch digestive power I have made a large number of experiments. In a series just completed I mixed 1 gm. portions of Samples 1 and 2 with water to make 100 c.c. volumes. Before making up to the final volumes 0.5 c.c. of normal sodium hydroxid was added to neutralize the slight acidity of the ferment as shown by phenolphthalein.

Of these mixtures 4, 6, 8 and 10 c.c. portions were mixed with 50 c.c. of 1 per cent. starch paste and incubated at 40 degrees to find the colorless end-point in the starch digestion, by the iodin test.

At the end of twenty-two hours the iodin reaction was as strong as at the beginning, indicating no appreciable starch digestion.

To the flasks in which no digestion had taken place under these conditions, 5 mg. of a pancreas ferment was added. This gave an almost immediate conversion to the colorless end-point. This ferment was a sample of Holadin which had been in the laboratory about a year. The 5 mg. com-

pleted the reaction to the colorless end-point in less than ten minutes.

In a similar test I used 2 gm. of Lactopeptine No. 3, made up to 100 c.c. with 1.2 c.c. of normal alkali. Ten and 15 c.c. portions were incubated with 50 c.c. of 1 per cent. starch paste through twenty hours at 40 degrees with no apparent result. The Holadin then added, 5 mg. being used, completed the conversion in less than ten minutes.

This shows that the medium was a proper one for the test and that the Lactopeptine must be extremely weak. No sugar tests were made because the Lactopeptine contains milk sugar to the extent of about 60 per cent.

Similar results for both protein and starch digestives have been obtained in a large number of experiments. These here quoted show that the ferment activity of the preparation is so low as to merit no recognition practically. The digestion of a few milligrams of fibrin or starch after many hours of contact, while being perhaps scientifically possible, is of no value when we come to a consideration of the use of such bodies as digestive ferments in medicine.

The amount of lactic acid or "loosely combined HCl" present in Lactopeptine is very small, since the total acid which may be titrated by sodium hydroxid and phenolphthalein is measured by 0.5 c.c. of the normal hydroxid for 1 gm. of the Lactopeptine powder, in the mean. In different samples examined the range was found to be from 0.41 c.c. to 0.6 c.c. Tests with methyl orange, methyl red and other indicators showed that the free acidity is but trifling; if the whole of this acid, as measured by phenolphthalein, were calculated to HCl, the amount would be too small to have any appreciable physiologic activity, in view of the daily dose recommended, 10 to 20 grains of the powder.

Report of Referee B

The following table gives a summary of the results of my investigations on Lactopeptine. The numbers in the extreme left-hand column are the manufacturer's identifying marks. These, it is assumed, run serially, the higher numbers indicating the fresher specimens.

TABLE SHOWING ENZYMIC POWER OF LACTOPEPTINE PREPARATIONS

	Amylase	Pepsin	Rennin	Trypsin	Lipase
2275	—	+	+	—	—
2301	—	+	+	—	—
2312	—	+	+	—	—
2348	—	+	+	—	—
2352	—	+	+	—	—
2364	—	+	+	+(?)	—
2374	—	+	+	—	+(?)
2383	—	+	+	+	+(?)
1638 (tablets)	—	+	+	—	—
Pancreatin (Old)	—	..	..	++	—

The conclusions in the foregoing summary depend on the following criteria:

Amylase: removal of starch (paste), *small in proportion to begin with.*

Pepsin: solution of small shreds of *fresh* fibrin in acid media.

Rennin: curdling of milk in moderate excess.

Trypsin: solution of small shreds of *fresh* fibrin in neutral and alkaline media, and tryptophan test.

Lipase: coloration of litmus-milk; exact *color* controls.

All tests were suitably controlled. The responses for pepsin were weak even when compared with those of old pepsin preparations.

In the table above, the interrogation points in parentheses (?) refer to results that were obtained after treatment for from twelve to twenty-four hours and indicates that the change was slight at best and of no practical import.

PROPRIETARY DIGITALIS PREPARATIONS

Report of the Council on Pharmacy and Chemistry

(From The Journal A. M. A., Dec. 4, 1915, p. 2024)

The Council has authorized publication of the following expression of its views. W. A. PUCKNER, Secretary.

It is becoming increasingly apparent that the tincture of digitalis produces the full therapeutic effects of digitalis, and that when it is properly made it is as stable as any liquid preparation of digitalis now available; and that the tincture has the systemic side actions of digitalis, including the emetic, in no greater degree than the various proprietary preparations of this drug to be found on the market.

While in itself the market price of a valuable therapeutic agent is of comparatively little moment, the fact remains that the high price at which many of the proprietary preparations of digitalis are sold — often 100 times that of an equivalent amount of the drug — serves as a constant stimulus to the exploitation of these with extravagant claims, and it is commonly sought to enhance their reputation by exaggerating the disadvantages of the official drug and its preparations.

The Council especially emphasizes the fact that this statement is not intended to lessen the efforts that are being made to find new and better preparations of digitalis; its protest is against the deliberate misrepresentations of those manufacturers who seek to magnify the difficulties in the

use of digitalis, by therapeutic exaggeration on the one hand, and by an exaggeration of the side actions of digitalis and the instability of its preparations on the other.

Strophanthin and crystalline ouabain are now available in sterile solution in ampules, and afford a convenient means of promptly securing the cardiac action by intramuscular or intravenous injection.

PROTONUCLEIN AND PROTONUCLEIN BETA

Report of the Council on Pharmacy and Chemistry

(From The Journal A. M. A., Jan. 1, 1916, p. 48)

The Council has adopted the following report and authorized its publication. W. A. PUCKNER, Secretary.

Protonuclein, with other products of Reed and Carnrick, was examined by the Council in 1907 and found ineligible for admission to New and Nonofficial Remedies. According to the patent specifications, it is prepared "from the thyroid and thymus glands, brain (pineal glands and pituitary body), bone-marrow, pancreas, spleen, liver, salivary glands, Brunner's glands, Lieberkühn's follicles and peptic glands." These various glandular bodies, it is said, are dried at a temperature below 130 F. (preferably between 100 and 110); the fat is removed by ether, the dried glands disintegrated, the connective tissue removed by sifting and the resulting powder coated with an ether solution of benzoin and mixed with milk sugar. The dose is three to ten tablets (9 to 30 grains) daily.

Protonuclein Beta is said to be produced by the addition to Protonuclein of an equal amount of nucleoplasm and protoplasm of the spleen. The dose is from two cubes (each 5 grains) three times a day to three cubes four times a day (30 to 60 grains daily).

Special advantages over ordinary nuclein are attributed to Protonuclein, in which, it is claimed, certain unaltered cells remain that are more easily assimilated by the leukocytes than are ordinary proteins, thus leading to a multiplication of cells. In the early advertising Protonuclein was claimed to be:

> ". . . an exact physiological product derived from the lymphoid structures of the body without the use of chemical agents. . . . So delicate is Protonuclein that any chemical agent is liable to disturb its cellular activity."

After its examination of the product in 1907 (THE JOURNAL, Oct. 5, 1907, p. 1198), the Council concluded that any dis-

tinction between the action of Protonuclein and that of ordinary nuclein was purely speculative and highly improbable. "If the active ingredients are really so unstable that they are destroyed by all chemical agents, as claimed, it seems impossible that the activity would be preserved when Protonuclein is given by mouth and therefore subjected to the very profound changes of digestion."

At that time the importance of thyroid as an ingredient had not been emphasized. The following year, however, Hunt and Seidell (THE JOURNAL A. M. A., Oct. 24, 1908) reported the results of an investigation which showed that Protonuclein was a diluted thyroid preparation, as skilfully disguised as in the antifats Rengo and Marmola. Hunt later pointed out (THE JOURNAL, Feb. 1, 1913, p. 384) that the amount of nuclein contained in a dose of Protonuclein probably would not have the slightest effect, especially when given by mouth.

The following are extracts from the Protonuclein advertising matter:

"For cancer, infectious fevers (measles, scarlet fever, typhoid and septicaemia) and as a prophylactic."

"Protonuclein: An ideal prophylactic for all infectious Diseases."

"A true alterative and tissue builder."

"The value of Protonuclein depends upon its ability to increase cell power and promote tissue strength. It is therefore needed whenever the organism is below the normal standard, more especially in Anaemia, Typhoid, Neoplasms and as a Prophylactic."

All the foregoing claims and recommendations are supposed to be based on certain alleged discoveries which the Council has previously characterized as "a tissue of vague speculations . . . in direct conflict with the known facts of physiologic chemistry." As for the third claim, Hunt and Seidell have commented on the danger of recommending thyroid, the most powerful tissue-destroying drug known, as a "tissue builder."

Protonuclein Beta, it is said:

". . . combines the reconstructive action of Protonuclein with the action of the vital principle of the spleen, making it a distinct product for use in all tubercular troubles, including phthisis, localized joint affections and scrofular conditions."

This product, according to the manufacturers, is based on the work of a certain Dr. Bayle of Cannes, France. Dr. Bayle said that he had treated tuberculous patients with fresh ground up spleen of hogs (25-100 grams per day), mixed with fruit preserve or bouillon; in cases in which this brought on gastro-intestinal disorders, extract of the spleen pulp was administered hypodermically. Bayle reported extraordinary

improvements in the physical and mental conditions of his patients even after a few days of this treatment; over 90 per cent. of his tuberculous patients, according to him, improved or were cured. This applied to all types and stages of tuberculosis in man. "With the spleen pulp treatment tuberculous glands disappear like syphilis lesions on administration of mercury and iodids."

This "spleen specific" of Bayle lacks scientific foundation; Bayle's own cases were not adequately controlled, and no notice has been taken of Bayle's report by experts on tuberculosis. Hence it practically lacks both confirmation and contradiction.

The spleen is invaded by tubercle bacilli quite as frequently as are the kidneys and the liver; it has no special toxic action on these bacilli. Nor is there any reason to believe that the end products of gastric and intestinal digestion of spleen pulp, after absorption into the blood, exert such toxic action. It cannot be assumed that these end products indirectly aid the healing processes through improved metabolism, for there is no evidence that they have any specific nutritive or stimulating action after such absorption. Altogether, what we know of the physiology and pathology of the spleen does not warrant us in looking for a "specific" against tuberculosis in this organ.

If, however, the known facts did justify any hope that the spleen might furnish such a specific, manufacturers would not be warranted in exploiting or physicians in prescribing spleen products as a remedy for tuberculosis until control experiments on animals had confirmed the therapeutic value of these products. In a chronic disease like tuberculosis, no conclusions that are scientifically valid can be drawn from clinical cases until many cases have been observed for years under suitable conditions. Right here it may be said that the clinical "evidence" offered in favor of Protonuclein Beta is worthless. The observations which have been reported on this product are not such as to permit any valid final conclusions to be drawn with regard to its value.

The rational method of proving the worth of an alleged new specific such as this is by animal experimentation. So far as we know, neither Dr. Bayle nor the Reed and Carnrick company has performed any such experiments with "spleen pulp" or Protonuclein Beta; nor are we aware that any competent investigator has done so. There is, to the best of our knowledge, no scientific evidence on which to base the claims for Protonuclein Beta.

The Council reaffirms its former action with regard to Protonuclein. The objections made to Protonuclein apply with equal force to Protonuclein Beta. In view of the lack of evidence, the claims for Protonuclein Beta are unwarranted and the product is ineligible to N. N. R. on account of noncompliance with Rules 1, 6 and 8.

DIGITALYSATUM

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., Jan. 8, 1916, p. 135*)

The Council has adopted the following report and authorized its publication. W. A. PUCKNER, Secretary.

Digitalysatum is sold in the United States by Ernst Bischoff Company, Inc., New York. The firm claims that it is a dialysate prepared from the juice of freshly gathered digitalis, containing all the active principles, and representing the fresh plant weight for weight. It is said to be standardized physiologically and to contain 12 per cent. alcohol. Sterisol-Digitalysatum, intended for injection, appears to be the "dialysate" without alcohol, diluted with equal parts of physiologic sodium chlorid solution. The Council some years ago found both products ineligible for New and Nonofficial Remedies because of unwarranted therapeutic claims. The preparations are still being advertised to physicians under claims which imply superiority to all other digitalis preparations. For instance:

"Digitalysatum is the diuretic *par excellence* in cardiac insufficiency . . ."

"Digitalysatum as a diuretic and cardiac stimulant is in a class by itself, being quick of action, uniform in strength, and well tolerated."

"Digitalysatum differs from other forms of digitalis in these respects: . . . Digitalysatum is free from fat, resins and colloids, and is therefore well-borne by sensitive patients—the young and the feeble—and is quickly absorbed and eliminated. . . ."

The Council has elsewhere[1] expressed the conviction that tincture of digitalis produces the full therapeutic effects of digitalis; that, when properly made, the tincture is as stable as any liquid preparation of digitalis now available, and that attempts to enhance the reputation of proprietary products by exaggerating the disadvantages of the official preparation are to be deplored. No adequate evidence is offered of the claimed superiority of action of Digitalysatum.

1. Report on Proprietary Digitalis Preparations, THE JOURNAL A. M. A., Dec. 4, 1915, p. 2024.

By implication, the claim is made that Digitalysatum is superior to other digitalis preparations in respect to toxicity:

"Free from fat, resins and colloidals, it is always well borne and is quickly absorbed and eliminated. No case of toxic accumulation (faulty elimination) has ever been reported."

That Digitalysatum is free from the dangers of toxic cumulation is highly improbable; in fact, it is inconsistent with the statement that the preparation contains all the constituents found in the fresh plant. Even if instances of cumulative action have not been reported this does not prove that such cumulative action does not occur. The tincture of digitalis has the systemic side-effects of digitalis in no greater degree than the various proprietary preparations. Attempts to create the impression that Digitalysatum possesses all the virtues of digitalis without its chief disadvantage are to be condemned as likely to lead to incautious use of the preparation.

These exaggerated claims are in the main made indirectly, but they are none the less inimical to sound therapy. The Council therefore declared Digitalysatum ineligible for New and Nonofficial Remedies and voted that this report be published.

HYDROPSIN

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., Jan. 8, 1916, p. 135*)

The Council has adopted the following report and authorized its publication. W. A. PUCKNER, Secretary.

Hydropsin is marketed by the Ernst Bischoff Company, Inc., New York. Its composition is thus described:

"Hydropsin is the standardized dialysate of Digitalis purpurea, Betula alba, Scilla maritima, Juniperis communis, and Herniaria glabra; or, stated otherwise, it is the juice of these drugs, dialyzed and physiologically standardized."

"Each fluid dram represents Digitalysatum 7 gtts., and 2 gtts. each of the dialysates of Betula, Herniaria, Juniper and Scilla."

The composition of Hydropsin must be considered essentially secret since the amounts of the several constituent drugs in a given amount of "dialysate" are not disclosed. The active principle of juniper is a volatile oil which is practically insoluble in water; it is difficult to believe that the "juice" of juniper submitted to dialysis could contain any material amount of the active constituent. No information is given as to the method used whereby the several dialysates are "physiologically standardized." It therefore

remains to be proved that the manufacturer of Hydropsin possesses any method whereby the dialysates of juniper (Juniperis communis), birch (Betula alba, the common European birch) and knot weed (Herniaria glabra) are so standardized. The claim is made that:

"Herniaria has long been recognized as one of the most valuable drugs in the treatment of dropsical affections due to cardiac impairment."

On the contrary, Herniaria belongs to that large class of drugs which have been tried, found wanting and abandoned. It is a very old remedy, and the claims made for it are an inheritance from the early herbalists, with whom it was very popular. According to King's American Dispensatory, it was "principally employed to cure *hernia* (hence its name) and to increase the flow of urine. It was also said to increase the flow of bile. . . . Internally and externally, it was praised in *snake-bites,* and the powdered plant was employed to kill maggots on unhealthy *sores* of horses. It was reputed to 'crush' and expel calculi from the kidneys and bladder. . . ."

The Ernst Bischoff Company says that:

"Betula exerts both an antiseptic and stimulating influence on the urinary passages and is particularly serviceable where a catarrhal condition of the bladder exists. When combined with other diuretics, as in Hydropsin, the drug affords highly satisfactory results in the treatment of ascites, cardiac dropsy and hydrothorax."

Birch is another drug which has been discarded. Few textbooks on materia medica even mention it. That it can materially affect the action of such powerful drugs as squill and digitalis is exceedingly doubtful.

An unwarranted implication—that in this preparation the powerful drugs digitalis and squill have been deprived of their dangerous qualities—is the assertion:

"Dialysis, removing all resins and colloidals, results in better tolerance on part of sensitive patients, and in more rapid absorption and elimination; which, in turn, means early therapeutic effects and little or no fear of toxic accumulation."

That removal of colloids and resins materially affects the tolerance of these drugs is improbable. To claim that because of their removal, there need be "little or no fear of toxic accumulation" is utterly without warrant. The claim that one preparation containing digitalis is less likely to produce cumulative effect than any other digitalis preparation is contradicted by a mass of evidence.

It is claimed that Hydropsin affects "favorably all forms of DROPSY or Edema that are at all amenable to medical

treatment." There can be no question but that squill and digitalis, or, better, either singly, used in suitable cases, may relieve dropsical effusions; but to claim that such a complex mixture as Hydropsin can favorably affect all forms of dropsy that are amenable to medical treatment is on its face unwarranted.

The claim is made that:

"By reason of its unusual potency and relative harmlessness, Hydropsin may be employed to great advantage in all cases where it is desirable to increase the volume of urine without injury to the renal structures."

On the basis of the claimed composition, the action of Hydropsin must be essentially that of digitalis or of digitalis and squill. Consequently, if it possesses "unusual potency," it cannot possess "relative harmlessness," and vice versa. Neither digitalis nor squill should be employed "in all cases" of nephritis, even if it is "desirable to increase the volume of urine."

The composition claimed for Hydropsin brands it as an irrational mixture in which potent drugs are combined with, and more or less covered up by, others that are obsolete and inefficient. The name, instead of indicating its composition, suggests diseases in which it may be thoughtlessly and indiscriminately used. The claim that the danger of toxic or cumulative action has been removed, if accepted by physicians, tends to uncritical use with possible disastrous results. Hydropsin is ineligible for New and Nonofficial Remedies because of conflict with Rules 1, 2, 6, 8 and 10.

SO-CALLED SECRETIN PREPARATIONS

Report of the Council on Pharmacy and Chemistry

(*From The Journal A. M. A., Jan. 15, 1916, p. 208*)

The Council authorized the following report for publication, and voted to endorse the work of Professor Carlson discussed therein. W. A. PUCKNER, Secretary.

The Council has not accepted for inclusion in New and Nonofficial Remedies any preparations said to contain secretin or prosecretin as their active ingredient. A report giving the reasons for the rejection of one (the first of the so-called secretin preparations marketed) was published early last year;[1] an article on secretin, based on work undertaken at

1. Secretogen, THE JOURNAL A. M. A., May 1, 1915, p. 1518.

the request of the Council on Pharmacy and Chemistry, is now published.[2]

Lest the appearance of this detailed study of secretin, after the rejection of so-called secretin preparations, should be interpreted (as manufacturers whose products have been rejected have endeavored to interpret such action) as a case of first condemning a preparation and then getting the facts, the Council's methods, and their application in this case, may be briefly stated. The Council maintains that, when a manufacturer places a product on the market, the burden of proof is on that manufacturer to show that the properties of his product are in accordance with his claims for it. As stated in the introduction to N. N. R., "it is . . . manifestly impossible for the Council to investigate the composition of every complex pharmaceutical mixture, or to check thoroughly every therapeutic claim; it can give only an unbiased judgment on the available evidence." Acting on this principle, the Council examined the claims made for Secretogen, an alleged secretin product manufactured by the G. W. Carnrick Company. The conclusion was that these claims were in absolute conflict with the available evidence as to the action of secretin.

It is not necessary to review this subject again. It will suffice to state that the claims made for Secretogen rest on two fundamental propositions: (1) that deficiency of secretin (or, rather, of prosecretin) in the intestinal mucosa is a factor in gastro-intestinal diseases; (2) that secretin given by the mouth is absorbed and produces increased secretion of the pancreatic and intestinal juices and of the bile.

From an examination of the evidence available, including that submitted by the manufacturers, the Council concluded: "1. No evidence has been presented that the absence of secretin is a cause of gastro-intestinal disease. 2. There is no evidence that secretin in any form is physiologically active when administered by mouth." That these conclusions were justified is shown again by the review given by Carlson of the literature, much of which was also reviewed in the Council's previous report.

Since the claims of the Carnrick Company were not supported by any satisfactory evidence, no further investigation on the Council's part was necessary to warrant rejection of the product. The Council did not undertake to determine, for instance, whether or not Secretogen and similar products actually contain secretin; the determination of this point was

2. Carlson, Lebensohn and Pearlmann: Has Secretin a Therapeutic Value? THE JOURNAL A. M. A., this issue, p. 178.

immaterial here, in view of the conclusiveness of the evidence that secretin given by mouth has no physiologic action.

Since firms other than the G. W. Carnrick Company are manufacturing alleged secretin preparations, and since recommendations for the use of secretin preparations in gastrointestinal diseases have even crept into textbooks, it seemed desirable to obtain further information on certain points. The Council therefore requested Prof. A. J. Carlson of the University of Chicago to check the results of previous investigators with regard to the action of secretin administered by mouth or directly into the intestine, and, in addition, to investigate the secretin content of certain alleged secretin preparations.

Carlson and his co-workers, like all previous investigators, found that secretin given by the mouth, or introduced even in enormous doses directly into the intestine, is entirely inactive. They also found that marked destruction of secretin followed contact for one minute with human gastric juice and that secretin is rapidly oxidized and rendered inert in contact with the air.

Further, they were unable to demonstrate the presence of secretin in samples of Secretogen and another supposed secretin preparation (Duodenin) bought on the open market. In the case of Secretogen there was one exception: one bottle was found which contained a little secretin, but it was necessary to administer (by intravenous injection, of course) the entire contents of the bottle (100 tablets) to obtain "a small but unmistakable secretin reaction."

In these studies the methods employed were those by which secretin was discovered. It is only by the use of such methods that the presence or absence of secretin can be determined. Apparently the manufacturers who place so-called secretin preparations on the market do not make use of these methods, by which alone even the composition of their products can be determined.

Carlson and his collaborators conclude:

"There is as yet no reliable evidence that lack of secretin is a primary or important factor in any disease. Even should this be established, secretin therapy, to be effective, must be intravenous. Secretin has not yet been prepared in sufficiently pure state to render possible intravenous injection in man without injurious effects. And even when this is attained, the very fleeting action of secretin will in all probability render secretin therapy as futile in all the diseases in which it is theoretically indicated as epinephrin therapy is in Addison's disease."

In short, secretin is as ineffective taken by mouth as it would be rubbed on the skin.

The referee recommends that the work of Professor Carlson be endorsed.

HAS SECRETIN A THERAPEUTIC VALUE?*

(*From The Journal A. M. A., Jan. 15, 1916, p. 178*)

A. J. Carlson, Ph.D., J. E. Lebensohn, M.S., and S. J. Pearlman, B.S.
Chicago

It is well established that acid chyme in the duodenum is the normal stimulus to the secretion of pancreatic juice.[1] Interaction of the acid with the duodenal mucosa liberates into the blood stream a substance which, circulating through the pancreas, excites the latter to activity. This exciting substance has been termed "secretin." It can be prepared artificially by macerating duodenojejunal mucosa in 0.4 per cent. hydrochloric acid, neutralizing the boiling mixture, and filtering. A few cubic centimeters of the filtrate injected into a vein produce invariably a powerful secretion of pancreatic juice.[2] That a "chemical messenger" is at the basis of the duodenal acid reflex has been proved by even more crucial experiments—transfusion (Wertheimer,[3] Enriquez and Hallion[4]), cross circulation (Fleig,[5] Matuso[6]), and perfusion of the isolated pancreas (Huston[7]).

PROPERTIES OF SECRETIN

Prosecretin.—Secretin is soluble in water, yet a watery extract of intestinal scrapings is without action,[2] even after being submitted to acid treatment.[8] Starling therefore holds that secretin exists in the intestinal mucosa in an inactive

* From the Hull Physiological Laboratory of the University of Chicago.

* This investigation was undertaken at the request of the Council on Pharmacy and Chemistry. The following report, having been submitted to the Council, received its endorsement (see preceding report of the Council on Pharmacy and Chemistry, "So-Called Secretin Preparations").

1. Pawlow: The Work of the Digestive Glands, 1912.
2. Bayliss and Starling: Jour. Physiol., 1902, xxviii, 325.
3. Wertheimer: Compt. rend. Soc. de biol., 1902, liv, 475.
4. Enriquez and Hallion: Compt. rend. Soc. de biol., 1903, lv, 233, 363.
5. Fleig: Arch. internat. de Physiol., 1910, x, 206.
6. Matuso: Jour. Physiol., 1913, xlv, 477.
7. Huston: Ann. et bull. Soc. roy. de sc. méd. et nat., 1912, lxx, 178.
8. Starling: Lancet, London, 1905, ii, 433.

form, as "prosecretin." The content of the intestine in prosecretin decreases from the duodenum down, so that one is unable to demonstrate any prosecretin in the last 2½ feet of the ileum. Prosecretin is insoluble in water, acetone, absolute alcohol or ether. Secretin, on the other hand, is readily soluble in water, normal salt solution and diluted alcohol (70 per cent.), but likewise insoluble in absolute alcohol and ether.

Preparation.—All of the more dissociated acids liberate secretin from intestinal mucosa on boiling. Their action is dependent on the degree of dissociation,[9] carbonic and boric acids being inactive.[10] Secretin can also be prepared with strong soaps (from 10 to 30 per cent. sodium oleate), alcohol (70 per cent.,[11] 0.6 per cent. sodium chlorid[6]). The acid and soap in the duodenum produce secretion; there is no necessary correspondence between the action of a substance in the intestine and that obtained by injection after boiling mucosa with it. The sodium chlorid, bile, maltose and glucose produce some secretion by the latter method yet none by the former.[6] On the other hand, ether, chloral and oil of mustard excite secretion when in the intestine, but no secretin can be prepared from boiled mucosa by their action. The irritation of the lining cell has produced the necessary hydrolysis.[8] In well-controlled experiments, Wertheimer and LePage[12] found that after the introduction of acid, secretion is secreted into the lumen of the intestine. Matuso[8] confirmed their results, and found this a satisfactory method for the preparation of secretin. It is said that secretin can be obtained by merely boiling the mucosa with water, but the results are inconstant.[13]

Action.—Secretin is an excitant not only of the pancreatic juice but also of the liver and the intestinal mucosa. The flow of bile is markedly accelerated (Henri and Portier,[14] Enriquez and Hallion[15]), likewise that of succus entericus (Delezenne and Frouin,[16] Bottazzi and Gabrielli[17]), and intestinal peristalsis is stimulated (Enriquez and Hallion,[18] Falloise[19]). Injections of secretin produce a marked vaso-

9. Frouin and Lalou: Compt. rend. Soc. de biol., 1911, lxxi, 189.
10. Camus: Compt. rend. Soc. de biol., 1902, liv, 442.
11. Fleig: Jour. de physiol. et de path. gén., 1904, vi, 32, 50.
12. Wertheimer and LePage: Jour. de physiol. et de path. gén., 1902, iv, 1061, 1070.
13. Stepp: Jour. Physiol., 1912, xliii, 441.
14. Henri and Protier: Compt. rend. Soc. de biol., 1902, liv, 620.
15. Enriquez and Hallion: Presse méd., 1903, i, 105.
16. Delezenne and Frouin: Compt. rend. Soc. de biol., 1904, lvi, 319.
17. Botazzi and Gabrielli: Arch. internat. de physiol., 1905, cxi, 156.
18. Enriquez and Hallion: Bull. gén. de thér., 1911, clxii, 202.
19. Falloise: Bull. de l'Acad. roy. de Belgique, 1902, v, 945.

dilatation, but the secretory effect is independent of the blood pressure changes. The pancreas is not readily fatigued by secretin. Bayliss and Starling[2] have obtained undiminished flow after eight hours of continuous injection. Our experience confirms this result. Also, equal doses of secretin give corresponding results at various intervals. Moreover, anesthesia does not affect the flow. Secretin is unrecoverable from the glands even after two hours of continuous injections.[22] The juice obtained by secretin has been subject to many studies.[23] It is of high alkalinity (about seventh normal), contains all the pancreatic ferments, and corresponds in all respects to the juice obtained in digestion from permanent pancreatic fistulas.[24]

Specificity.—In a maceration of the duodenojejunal mucosa, such as we have in secretin, the known substances are proteoses and peptones, acid amins, bile salts, beta-imidazolethylamin, cholin, gelatin and inorganic salts. These substances, individually and severally, together with their derivatives, are devoid of secretory action. Chemically, secretin is then a specific entity. But like epinephrin, in its distribution, it is nonspecific. Active preparations have been made from an extraordinary variety of animals among the different classes of vertebrates (Camus,[25] Bayliss and Starling,[26] Chapman[27]). It is likewise found in the new-born and in the fetus.[28] Its action, however, like its chemical composition, is markedly specific. It stimulates the flow of pancreatic juice, bile and succus entericus. Its effect on the gastric glands is negative, and on the saliva likewise.[29] On the other hand, no other extracts produce pancreatic secretion. Dr. Koch, who, in collaboration with Dr. Keeton and Dr. Luckhardt, has done the most recent work on gastrin[30]

20. Bayliss and Starling (Note 2). Matuso (Note 6). Arch. internat. de physiol., 1911, x, 335.
Terroine: Compt. rend. Soc. de biol., 1909, lxvii, 36. Zunz: Arch. internat. de physiol., 1909, viii, 181. Lalou: Jour. de physiol., 1912, xiv, 465.
21. Launoy: Arch. internat. de Physiol., 1906, iii, 62. Morel and Lalou: Jour. de physiol., 1912, xiv, 465.
22. Dixon and Hamill: Jour. Physiol., 1909, xxxv, 314.
23. Bayliss and Starling: Jour. Physiol., 1904, xxx, 61. Bierry: Compt. rend. Soc. de biol., 1907, lxii, 433. Bierry and Terroine: Compt. rend. Acad. de sc., 1905, cxli, 146. Lalou: Compt. rend. Acad. de sc., 1910, xxix, 824. Morel: Compt. rend. Soc. de biol., 1909, lxvii, 36. Strassano and Billoro: Compt. rend. Soc. de biol., 1902, liv, 937.
24. Bayliss and Starling (Note 23).
25. Camus: Jour. de physiol. et de path. gén., 1902, iv, 998.
26. Bayliss and Starling: Jour. Physiol., 1903, xxix, 174.
27. Chapman: Proc. Linnaean Soc., New South Wales, 1905, i, 92.
28. Camus: Compt. rend. Soc. de biol., 1906, lxi, 59. Hallion and Lequex: Compt. rend. Soc. de biol., 1906, lxi, 33.
29. Derouaux: Arch. internat. de physiol., 1905, iii, 44. Lambert and Myer: Compt. rend. Soc. de biol., 1902, liv, 1044. Starling: Lancet, London, 1905, ii, 501.
30. Keeton and Koch: Am. Jour. Physiol., 1915, xxxvii, 481.

(a substance that most nearly resembles secretin) and has isolated an extremely active preparation, finds that gastrin injection has likewise no effect on the pancreas. Camus and Gley,[31] with crude preparations, had previously obtained a similar result.

Lability.—Neutral secretin is but feebly attacked by a temperature of 100 C. If heated in an autoclave (so as to prevent oxidation), this temperature can be continued for thirty minutes without any change in its activity. Increasing the temperature increases the speed of destruction, so that at 140 C. the destructive action is marked.[32] Autoclaving at 15 pounds for fifteen minutes, as in ordinary sterilization of culture mediums, produces, we found, a distinct though not serious decrease in activity. Secretin acidified to fifth-normal with hydrochloric acid loses 60 per cent. of its activity on fifteen minutes boiling. Secretin, alkalinized to fifth-normal with sodium hydroxid loses 95 per cent. of its activity in five minutes' boiling; decreases to a trace in thirty minutes, and disappears entirely in sixty minutes. At room temperature, with fifth-normal alkalinity, 80 per cent. of secretin is destroyed in eight hours.[32] The destruction probably means a secondary cleavage of the secretin molecule itself.

Secretin is oxidized readily. If left standing uncovered for a summer's day, the preparation will be inactive.[22] Even if kept in the ice-chest (no other precaution being taken), its activity is lost in a very few days. Sunlight undoubtedly hastens the oxidative process. If care is taken as to sterility, however, and the secretin is kept in the ice-chest, well stoppered and in a dark flask, it will retain its activity for several weeks.

Dixon and Hamill[11] claimed that secretin disappears quantitatively on passage through a Berkefeld filter at 5 mm. pressure. Lalou,[21] using higher pressure, was unable to confirm the finding, but obtained a marked decrease in activity. Our results are in accord with those of Lalou.

Analogy to Epinephrin.—The analogy of secretin to epinephrin does not generally receive enough emphasis. Both substances are nonspecific in distribution, but specific chemically, and especially physiologically, epinephrin acting on the myoneural junctions, secretin on intestinal digestion. They are both relatively simple substances of low molecular weight, and subject to rapid oxidation whereby their properties disappear. The action in both cases is very transient. They are the two examples of what Starling calls the "acute

31. Camus and Gley: Compt. rend. Soc. de biol., 1902, liv, 648.
32. Lalou (Note 21). May: Jour. Physiol., 1904, xxx, 400.

hormones," in which it is essential that reaction take place immediately, and shall disappear as soon as the exciting cause is removed.[33]

CLINICAL USE OF SECRETIN

Diabetes Mellitus.—Moore, Edie and Abram[34] were the first to suggest a therapeutic value for secretin, having obtained favorable results with secretin administration in diabetes. They argued that the internal secretion of the pancreas *may* be stimulated by secretin, and that some cases of diabetes *may* be due to lack of this necessary excitant. Owing to the importance of the question, their announcement was followed quickly by numerous investigations by other observers. Previously, Spriggs, at the suggestion of Starling, had tried intravenous injections of secretin free from depressor substance in a diabetic patient, and had obtained negative results. Moore, Edie and Abram gave their secretin by mouth over long periods. Of the five cases cited in their first paper, two were negative. The third was that of a man, aged 25, who received daily 30 c.c. of secretin. After a latent period of three weeks, the sugar suddenly fell, and after four months the urine was sugar-free. Six months later a relapse occurred with the development of phthisis and death. The other two patients were a boy, aged 7, and a girl, aged 9, whose urine in from three to five weeks became sugar free during the secretin treatment in spite of severe diabetes. One of these patients later relapsed.[35] Bainbridge and Beddard[36] gave secretin a thorough trial in three cases with negative results, and are disposed to attribute the results of Moore to dieting. Dakin and Ransom[37] cited one case, secretin being given for twelve weeks, with negative results; Foster,[35] nine cases, all negative; Charles,[38] three cases, all negative. Crofton,[39] however, gave secretin a trial in one case with favorable results. Moore, Edie and Abram, in a later paper,[40] report a large number of cases tried with the majority of results negative, though in some cases an improvement in the digestion, and in certain cases an increase of weight was noted.

One method of testing the basis of Moore's theory would be by examining the prosecretin content of the intestine in

33. Starling: Proc. Roy. Soc. Med., 1914, viii, No. 4, Therap. and Pharm. Section, p. 29.
34. Moore, Edie and Abram: Biochem. Jour., 1906, i, 28.
35. Foster: Jour. Biol. Chem., 1906, ii, 297.
36. Bainbridge and Beddard: Biochem. Jour., 1906, i, 429.
37. Dakin and Ransom: Jour. Biol. Chem., 1906, ii, 305.
38. Charles: Med. Press and Cir., 1906, cxxxiii, 578.
39. Crofton: Lancet, London, 1909, clxxvi, 607.
40. Moore, Edie and Abram: Biochem. Jour., 1908, iii, 82.

diabetics. Bainbridge and Beddard found, in the paper referred to,[36] that from five of the six cases of diabetics examined postmortem, little or no secretin could be prepared; but in a subsequent report of seven cases,[41] they found only one in which the secretin obtained was scanty. The failure to obtain secretin in some cases they claim is probably due to the rapid postmortem degeneration of diabetic tissue. Evans,[42] in Starling's laboratory, found that in dogs made recently diabetic by total pancreatectomy, but little secretin could be obtained. Hedon and Lisbonne,[43] and Pemberton and Sweet[44] report, on the contrary, that the duodenum of diabetic dogs is rich in prosecretin. Bainbridge and Beddard,[41] working on a diabetic cat, likewise found prosecretin to be present in normal quantity.

Digestive Disturbances.—Secretin for digestive disturbance was first used in the "acid duodenal medication" of Enriquez.[45] This consisted in the giving of tartaric acid in thick keratin capsules, the acid not being liberated until the duodenum was reached, where it provoked the formation of secretin. "The secretin mechanism," he says, "is probably capable of pathologic disturbance as would result, for example, with diminished acidity of chyme, disturbance of the normal motility of the stomach or pylorus, or diminished prosecretin in the mucosa. Such a condition would produce disturbance of the pancreatic, biliary and intestinal secretions, and interfere with intestinal movements, with a clinical syndrome of intestinal dyspepsia as a result, among the chief and most constant symptoms of which would be constipation." "The acid duodenal medication" was submitted to wide clinical use, and very favorable results in certain obstinate cases of constipation were reported. In regard to "diminished prosecretin in the mucosa," Wentworth[46] has claimed that in infantile atrophy such is the condition, but Sweet and Pemberton[47] have found that the difficulty of preparing secretin from human duodenums is such as to render Wentworth's findings inconclusive.

Beveridge[48] suggests the use of secretin in *(a)* pyloric stenosis, *(b)* pancreatic insufficiency, *(c)* hepatic stimulation

41. Bainbridge and Beddard: Biochem. Jour., 1908, iii, 82.
42. Evan: Jour. Physiol., 1912, xliv, 461.
43. Hedon: Compt. rend. Soc. de biol., 1913, lxxiv, 375.
44. Pemberton, Ralph, and Sweet, J. E.: Further Studies on the Influence of the Ductless Glands on the Pancreas, Arch. Int. Med., May, 1910, p. 466.
45. Enriquez: Bull. du Lab. de biol. Appliq., 1904, ii, No. 2-No. 8.
46. Wentworth, A. H.: The Cause of Infantile Atrophy, THE JOURNAL A. M. A., July 20, 1907, p. 204.
47. Sweet, J. E., and Pemberton, Ralph: Experimental Observations on Secretin, Arch. Int. Med., February, 1908, p. 231.
48. Beveridge: Am. Med., 1914, xx, 255.

and cirrhosis of the liver *(d)* to stimulate peristalsis in colonic stasis, *(e)* in gastro-enterostomy and short-circuiting of the intestines. He claims to have used it in over a hundred cases with "brilliant results," and cites four typical histories. The G. W. Carnrick Company, which manufactures "Secretogen," an alleged secretin preparation, cites a number of authorities[49] as also recommending secretin for digestive disorders. Harrower, who is or was connected with the Carnrick Company, in clinical journals[50] has ardently advocated the use of secretin for a large number of maladies.

PHYSIOLOGIC CONSIDERATIONS

Throughout its clinical use, secretin has been given by mouth; *but its direct introduction into the intestine of a dog under anesthesia in even enormous quantities is without effect.* This fact, first observed by Bayliss and Starling,[2] was confirmed by Fleig,[51] and Matuso,[6] and our personal experiments have convinced us of its truth. Matuso found that ordinary secretin and that obtained from intestinal lumen gave equally negative results. Large quantities of active secretin, moreover, acidified to 0.2 per cent. hydrochloric acid, and left in the ileum for fifteen minutes, were still negative. Wertheimer and Duvillier,[52] in a previous paper on this subject, had likewise found that acid solutions of secretin (which might be considered more normal for the intestine than when neutral), when introduced into the ileum gave negative or inconstant results. They conclude that it is more likely that the pancreas does not respond to such minimal stimuli, than that the secretin is not absorbed.

The destructive action of the digestive enzymes leads us to believe that it is in inactive form that secretin is absorbed. Like epinephrin, it cannot pass through the digestive tract. Bayliss and Starling state that it is destroyed by one hour's tryptic digestion. Lalou[21] worked with the action on secretin of pepsin, dog's gastric juice, pancreatic juice, succus entericus and erepsin, and found in each case a destructive effect, even almost after mixing; and after five minutes over 75 per cent. of the activity had disappeared. Matuso[6] intro-

49. Lockwood, G. R.: Diseases of Stomach, 1913, Chapter on Achylia. Bassler, Anthony: Am. Jour. Gastro-Enter., 1914; Kemp, R. C.: Diseases of Stomach, Intestine and Pancreas, 1912. Reed, Boardman: Am. Jour. Gastro-Enter., October, 1912. Ewald (Therapie der Gegenwart, 1915, p. 5) reports favorable results with Secretogen in one of thirteen cases.

50. Harrower: Pediatrics, 1913, xxv, 430; New York Med. Jour., 1913, cxviii, 315; Arch. f. Verdauungskr., 1914, xx, 577.

51. Fleig: Arch. gén. de méd., 1903, cxci, 1482.

52. Wertheimer and Duvillier: Compt. rend. Soc. de biol., 1910, lxviii. 535.

duced 30 c.c. of active secretin into the intestine, removed it five minutes later, and found that no activity remained.

Other methods of administration have been tried. Subcutaneous injections are practically negative (Matuso,[6] Hallion[53]) and intrapleural injections are likewise negligible (Bayliss and Starling[26]).

Starling[33] finds that continued intravenous injections of secretin in a healthy dog produces after a time severe symptoms of collapse, which, he believes, are due to change in the intestinal mucous membrane caused by the entry and non-neutralization of the strongly alkaline pancreatic juice.

Intestinal digestion seems little affected in achylia gastrica (Stockton,[54] Ehrman and Lederer,[55] Bayliss and Starling[2]). This may be due to other secretin stimulants as fats, or to the action of the nervous mechanisms (Meltzer[56]).

THE DESTRUCTION OF SECRETIN BY HUMAN GASTRIC JUICE

We have carried out in detail experiments on the digestive effect of human gastric juice on secretin. Our results in every respect confirm the findings of Lalou,[21] who worked with commercial pepsin and dog's gastric juice, but are even more striking because of the much superior quality of pure human gastric juice.

Methods.—The human gastric juice was obtained from Mr. V., the gastric fistula case of our laboratory. The chemical and digestive characters of his juice are discussed in a recent paper.[57] In the different experiments, different samples of gastric juice were used. The secretin employed was always freshly prepared. Digestion was carried out in the incubator at 38 C. with the reaction of 0.4 per cent. acid, and the end of the period was marked by either boiling the mixture or (in the first two experiments) by turning the mixture alkaline. The action of the preparation, we proved, was not influenced by the method used. The dogs on which the preparations were tested were prepared for carotid blood pressure, injection into the external jugular vein, and cannula in the pancreatic duct, essentially the methods of Bayliss and Starling[2] being employed. The preparations were injected at body temperature after being neutralized and filtered. Except for the addition of normal salt solution instead of gastric juice, the control injections of secretin

53. Hallion: Presse méd., 1912, xx, 433.
54. Stockton: In Osler and McCrae's Modern Medicine, 1914, iii, 19.
55. Ehrman and Lederer: Deutsch. med. Wchnschr., 1909, xxxv, 879.
56. Meltzer, S. J.: The Factors of Safety in Animal Structure and Animal Economy, THE JOURNAL A. M. A., Feb. 23, 1907, p. 655.
57. Carlson: Am. Jour. Physiol., 1915, xxxviii, 248.

TABLE 1.—THE DESTRUCTION OF SECRETIN BY HUMAN GASTRIC JUICE

No. of Experiment	Quantity of Gastric Juice Used c.c.	Secretion of Pancreatic Juice in Drops							
		10 c.c. Secretin Control—Beginning Experiment	The Secretin after Incubation with Human Gastric Juice						10 c.c. Secretin Control—End of Experiment
			Dig. Time Hrs.	Secretion Rate	Dig. Time, Hrs.	Secretion Rate	Dig. Time, Hrs.	Secretion Rate	
1	2	28	6	0	4	0	2	0	16
2	2	110	2	7	1½	18	1	18	41
3	2	40	1	7	¾	7	¼	8	31
4	1	21	½	11	¼	12	1/60	14	18
5	8	20	½	1	¼	3	1/60	6	18
6	5	53	½	2	..	..	..	..	..

were submitted to exactly the same treatment as the other preparations.

Results.—Our results are embodied in Table 1. We assured ourselves before beginning the series that incubation of secretin with *boiled* gastric juice produced no change. It is to be noted in the table that each experiment is a unit complete in itself, beginning and ending with a control injection of secretin. *Special attention is called to the marked destruction that follows contact of human gastric juice with secretin for merely one minute.* In Experiment 4, using 1 c.c. of human gastric juice, the action fell to 14 drops from an original secretion of 21; in Experiment 5, using 8 c.c. of gastric juice, the action fell to 6 drops from an original secretion of 20. Of interest also is the rate at which we get *complete* destruction of secretin. This is practically 2 hours for 2 c.c. with secretin giving originally 110 drops (Experiment 2, Fig. 1), or 30 minutes for 5 c.c. with a secretin giving originally 53 drops (Experiment 6). These results are practically parallel, though they were obtained with different samples of gastric juice and in different experiments.

We also tried the effect of keeping the digestive time *constant* and varying the amount of gastric juice employed. Increasing the quantity of gastric juice used increases the quantity of secretin destroyed (Table 2).

TABLE 2.—EXPERIMENT 7*

Preparation	Pancreatic Juice Drops
10 c.c. secretin	20
10 c.c. secretin digested with 0.5 c.c. gastric juice	15
10 c.c. secretin digested with 3 c.c. gastric juice	13
10 c.c. secretin digested with 10 c.c. gastric juice	8

* The digestive time was kept constant at fifteen minutes. (The gastric juice used had been *diluted* with stomach washings.)

The reader will observe in Table 1 that the results obtained from the control injection of secretin at the beginning of the experiment is uniformly greater than that obtained after several injections of digested secretin.

In view of the established fact that equal quantities of secretin can generally be relied on to produce results,[21] one might suggest that the injections of the split products of secretin has inhibited to some degree the action of the pancreas. We can submit the data in Table 3 in support of this view, showing among other things that the action of secretin is not influenced by previous injections of inert depressor substances, though it is by the injection of the cleavage products of secretion. (The various injections in the experiments were made at about fifteen-minute intervals).

We have carefully analyzed the reaction in blood pressure that follows the injection of the various preparations. We find no constant effect. Digested secretin gives a fall in blood pressure that is at times less, at times equal, and at other times greater (Fig. 1) than that produced by the original preparation.

Besides the bearing that it has on *the therapeutic use of secretin,* this destructive action of the digestive enzymes is also of prime physiologic interest. Failure to realize it has led to misconceptions as to the intrinsic nature of secretin.

TABLE 3.—EXPERIMENTS 8 AND 9

Preparations	Pancreatic Juice Drops
Experiment 8:	
10 c.c. secretin, five injections of inert depressor substances.....	29
10 c.c. secretin, two injections of completely digested secretin....	28
10 c.c. secretin, eight injections of inert depressor substances....	16
10 c.c. secretin.....	16
Experiment 9:	
10 c.c. secretin (control, beginning of experiment).....	21
10 c.c. secretin, after thirty minutes incubation with 1 c.c. *boiled* gastric juice	27
10 c.c. secretin, after thirty minutes incubation with 1 c.c. *fresh* gastric juice	11
10 c.c. secretin (control, end of experiment).....	18

The findings of Lalou, confirmed by us, explain the anomaly that has led Delezenne[58] to put forward the antisecretin theory.

SECRETIN HAS NO ACTION WHEN GIVEN BY MOUTH

It is a constant claim that so many and complex are the factors concerned in physiologic processes, that it is not unusual for clinical deductions to establish themselves in the face of *a priori* laboratory dicta. We considered it desirable, therefore, to test the action of secretin, orally administered, in the most direct manner, and the one freest from possible criticism. With this in view, we performed a series of experiments on normal unanesthetized dogs having permanent pancreatic fistulas.

Method.—In the operations for permanent pancreatic fistulas we followed closely the technic developed by Pawlow,[59] and with excellent results. The dogs maintain themselves in splendid condition if proper care is taken. This consists in feeding them only with bread and milk, and giving sodium bicarbonate daily. The dogs were given this treatment in the evening so that experimental procedure might be carried on in the day with an empty stomach under constant conditions. Freshly prepared secretin in large quantities was given by

58. Delezenne and Pozerski: Jour. de Physiol., 1912, xiv, 540.
59. Pawlow: Ergeb. de Physiol., O., 1902, p. 266.

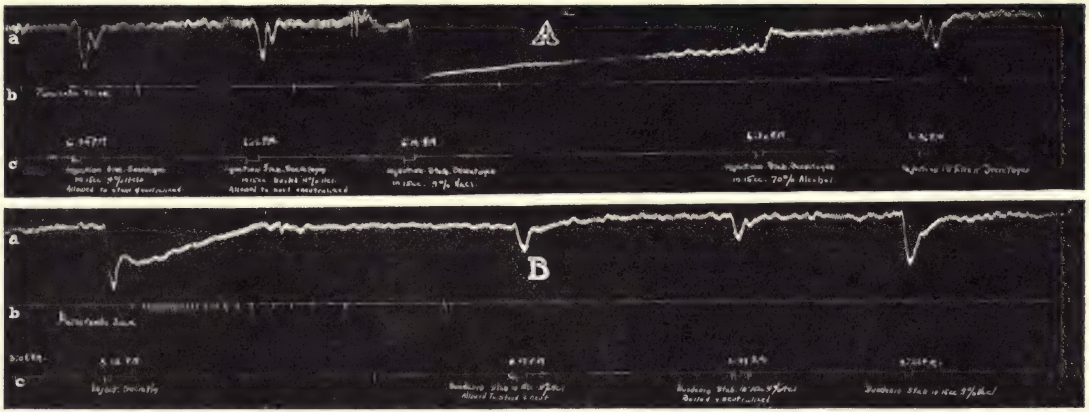


Fig. 1.—Tracings (reduced two-thirds) showing failure of Secretogen, Elixir Secretogen, and Duodenin to stimulate the flow of pancreatic juice even when administered intravenously in amounts three times greater than that recommended to be given by mouth. Dog: light ether anesthesia; cannula in the pancreatic duct; *a*, carotid blood pressure; *b*, flow of pancreatic juice in drops; *c*, signal showing where the intravenous injections were made. Tracing A: Reading from left to right, the five intravenous injections are: (1) three tablets of Secretogen digested with 15 c.c. 0.4 per cent. hydrochloric acid and neutralized; (2) three tablets of Secretogen boiled in 15 c.c. 0.4 per cent. hydrochloric acid and neutralized; (3) three tablets of Secretogen in 15 c.c. 0.9 per cent. sodium chlorid; (4) three tablets of Secretogen in 15 c.c. of 70 per cent. alcohol; (5) 15 c.c. Elixir Secretogen. Tracing B: reading from left to right, the four intravenous injections are: (1) 5 c.c. secretin made fresh from dog's duodenal mucosa; (2) three tablets of Duodenin digested in 15 c.c. 0.4 per cent. hydrochloric acid and neutralized; (3) three tablets of Duodenin boiled in 15 c.c. 0.4 per cent. hydrochloric acid and neutralized; (4) three tablets of Duodenin in 15 c.c. sodium chlorid (0.9 per cent.).

TABLE 4.—DETAIL OF TYPICAL EXPERIMENTS

Dogs with pancreatic fistulas, showing that secretin given by mouth has no action on the pancreas.

Material Fed by Stomach Tube	Rate of Secretion of Pancreatic Juice in c.c. Per Hour					
	Continuous Secretion Before Feeding			Continuous Secretion After Feeding		
	First Hour	Second Hour	Third Hour	First Hour	Second Hour	Third Hour
150 c.c. active secretin, slightly acid	6.5	3.6	3.9	20.0	6.0	8.0
150 c.c. active secretin, slightly alkaline	13.0	11.0	5.0	23.0	26.0	12.0
150 c.c. secretin passed through Berkefeld	7.8	7.5	7.4	23.0	13.0	11.0
150 c.c. extract of colon	11.6	12.0	11.4	30.0	19.6	14.8
150 c.c. extract of gastric mucosa	10.0	7.0	8.0	23.0	7.5	4.0
150 c.c. extract of muscle	6.9	11.0	6.4	35.0	5.0	7.0
150 c.c. 0.4% HCl (diluted to 250 c.c.)	6.0	8.0	4.0	33.0	36.0	17.0

TABLE 5.—SUMMARY OF EXPERIMENTS

Dogs with pancreatic fistula, weight 14 kg. Secretin given by mouth.

No. of Experiment	Material Fed	Rate of Secretion of Pancreatic Juice in c.c. Per Hour		Increase in c.c.
		Three Hours Before Feeding	Three Hours After Feeding	
3	Secretin slightly acid	5	11	6
5	Secretin slightly alkaline	24	30	6
4	Secretin passed through Berkefeld	18	23	5
1	Secretin exposed to sun for four hours	16	29	13
2	Extract of colon (rabbit)	19	29	10
3	Extract of gastric mucosa	14	23	9
3	Extract of muscle	8	16	8
2	Mixture of gelatin, peptone and salt	23	33	10
1	1 per cent. peptone solution	6	8	2
4	0.2 per cent. hydrochloric acid	13	37	24
3	Milk and bread	7	20	13

stomach tube to these dogs, and the response of the pancreas studied and compared with the response obtained from control preparations. The same preparation was generally not given on consecutive days.

Results.—We have data from six dogs with a total of seventy-six experiments. As shown in Table 4, the administration of secretin causes an increase in the flow of pancreatic juice, *but* the administration of inert substances as extracts of colon, gastric mucosa or muscle causes a like increase. The activity of the secretin may be reduced to a low value by exposure to sunlight, or filtering through a Berkefeld filter, yet the response of the pancreas is not correspondingly reduced. The secretion that occurs in the control cases, every one will admit, is but secondary to the production of gastric juice with its accompanying hydrochloric acid, that is, excited by virtue of the extractives and water in the preparations. Such, we can prove, is the only action of secretin. A mixture of gelatin, peptone and salt water, the chief incidental constituents of a secretin preparation, gives as striking results as ever obtained from secretin administration. Yet the objection may be made that the response of the pancreas that is due to the incidental constituents of secretin is maximal, and that the secretin consequently has no opportunity to display its particular potency. But, as inspection of the accompanying tables illustrate, the administration of hydrochloric acid shows that the response is by no means maximal. Let us cite a striking experiment. For three hours before the administration of hydrochloric acid, the secretion in cubic centimeters was respectively 29.4, 11.75 and 35.4 c.c.; for the three hours after, respectively 88.0, 49.0 and 40.5 c.c.

It is possible by large doses of sodium bicarbonate given shortly before the administration of a preparation so to depress the stomach that it does not respond with the usual production of hydrochloric acid. Under these conditions the administration of secretin is uniformly negative, but the administration of hydrochloric acid on the contrary still serves to increase the pancreatic secretion (Table 6).

COMMERCIAL PREPARATIONS OF SECRETIN

Secretogen and Elixir Secretogen.—The Carnrick Company offers Secretogen[60] for use in a large number of conditions. The following indications for the use of the preparation purport to be based on clinical tests covering a period of several years: dyspepsia, and the indigestions generally,

60. Secretogen, Report of the Council on Pharmacy and Chemistry, THE JOURNAL A. M. A., May 1, 1915, p. 1518.

TABLE 6.—SECRETIN IN EXPERIMENTAL "ACHYLIA GASTRICA"

Exp. No.	Material Fed	Rate of Secretion of Pancreatic Juice in c.c. Per Hour					
		Continuous Secretion Before Feeding *			Secretion After Feeding		
		First	Second	Third	First	Second	Third
1	150 c.c. secretin	8.7	7.5	6.8	3.0	1.0	4.8
2	150 c.c. secretin	4.5	6.5	10.0	6.0	7.5	7.6
3	150 c.c. secretin	15.6	8.1	16.0	3.9	4.9	2.9
1	150 c.c. 4% HCl (diluted to 250 c.c.)	9.8	7.0	6.0	65.1	28.0	7.1
2	150 c.c. 4% HCl (diluted to 250 c.c.)	17.4	13.5	17.0	34.0	18.0	20.0

* Five gm. Na HCO_3 given at beginning of each first two hours.

TABLE 7.—SUMMARY OF TYPICAL EXPERIMENTS SHOWING THE ABSENCE OF SECRETIN IN "SECRETOGEN" AND "ELIXIR SECRETOGEN" EXCEPT IN OCCASIONAL TESTS WHEN ADMINISTERED IN ENORMOUS DOSES

Dogs under ether anesthesia

Exp. No.	Quantity of Secretogen and Elixir Secretogen Used *	Secretion of Pancreatic Juice in Drops, Following Intravenous Injection						
		Control 10 c.c. Secretin	Secretogen in				Elixir	Control 10 c.c. Secretin
			Distilled Water	0.4% HCl	70% Alcohol	0.9% NaCl		
1	Secretogen, 1 tablet; Elixir, 15 c.c.	109	0	0	0	0	0	69
1	Secretogen, 6 tablets	...	..	0	..	..	..	..
2	Secretogen, 3 tablets; Elixir, 15 c.c.	16	0	0	0	0	1 (?)	16
3	Secretogen, 5 tablets	...	..	1 (?)	..	..	..	..
4	Secretogen, 25 tablets	14	..	1 (?)	..	..	..	8
5	Secretogen, 100 tablets	110	..	..	..	21	..	67
6	Secretogen, 100 tablets; Elixir, 125 c.c.	19	..	5	..	1	2 (?)	8
7	Elixir, 50 c.c.	...	..	..	..	..	1 (?)	..

* One to three tablets is (according to the label) the therapeutic dose of Secretogen; 4 to 12 c.c. the dose of Elixir Secretogen.

fermentative disorders, gastric catarrh, flatulence, nausea; pancreatic insufficiency, intestinal indigestion; gastric secretory deficiencies, apepsia; constipation and hepatic torpor; intestinal stasis; diarrhea; infantile diarrhea, "summer complaint," marasmus, inanition and malnutrition; gastric atony and dilatation; cholecystitis and gallstones; nephritis, neurasthenia, cachexia and cancer; epilepsy and high blood pressure. Testimonials are presented as to results in most of these conditions.

A quantity of "Secretogen" and "Elixir Secretogen" was bought in the open market, and the preparations were tested on suitably prepared dogs. The tablets were ground, thoroughly macerated with the solvent used (water, normal salt solution, alcohol, or 0.4 per cent. hydrochloric acid), and filtered. If hydrochloric acid was used, the pulverized tablets were boiled with it, in the manner that secretin is made from duodenal mucosa, and the preparations neutralized previous to injection. The injections were made in from 15 to 20 c.c. of the solvent. All the operations were carried on immediately before the experiment, and as rapidly as possible, so as to avoid oxidation. The Elixir Secretogen was injected directly, without dilution.

Results.—In only one case was a slight response obtained; the others gave none. Small and large doses were equally inert (Table 7, Figs. 2, 3). The preparations, though inert, always produced a depression in blood pressure, sometimes even greater than that caused by active secretin. Among our many tests, one bottle was found, however, to be a little different from the rest (Experiment 4). Its entire content, 100 tablets, had been ground and boiled in 0.9 per cent. sodium chlorid. The extract on injection was found to have a small but unmistakable secretin reaction, equivalent to about 2 c.c. of the control secretin used. But repeated experiments were unable to duplicate this result. The "Secretogen" and "Elixir Secretogen" were all supposedly fresh preparations, the retail drug store informing us that a fresh supply was obtained from the wholesale house each week.

Secretogen, then, contains practically no secretin, and even if it did contain secretin, it can have no effect on the pancreas when taken by mouth. The indications for Secretogen, therefore, are based on false premises, and the testimonials are worthless.

Duodenin.—This is a preparation manufactured by Armour & Company, which purports to be "secretin plus enterokinase." The claims for this product are similar to those for Secretogen, but somewhat less sweeping. According to the manu-

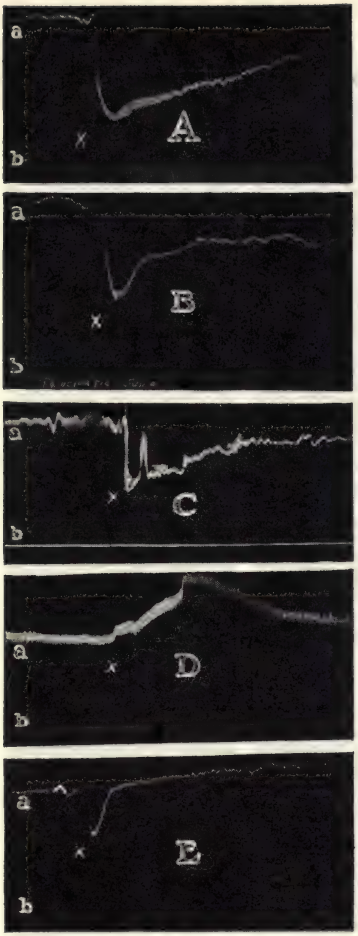


Fig. 2.—Tracings (reduced one-half) showing no stimulation of the pancreas by Secretogen, Elixir Secretogen, and Duodenin, even when administered intravenously in quantities one hundred times greater than the therapeutic dose by mouth. Dog: Light ether anesthesia; cannula in the pancreatic duct; *a*, carotid blood pressure; *b*, flow of pancreatic juice in drops. Tracing A: at *x*, intravenous injection of 10 c.c. secretin prepared from duodenal mucosa of dog. Tracing B: at *x*, intravenous injection of 100 tablets of Secretogen digested with 0.4 hydrochloric acid and neutralized. Tracing C: at *x*, intravenous injection of 100 tablets of Secretogen, prepared as in Tracing B. Tracing D: at *x*, intravenous injection of 50 c.c. Elixir Secretogen. Tracing E: at *x*, intravenous injection of 100 tablets of Duodenin (dissolved in 0.9 per cent. sodium chlorid).

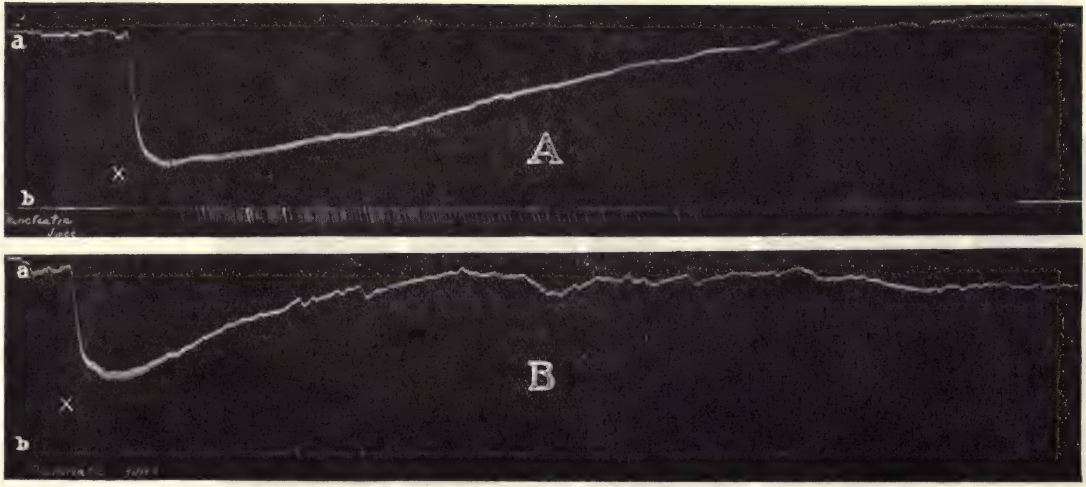


Fig. 3.—Tracings (reduced one-half) showing practically complete destruction of secretin by the gastric juice. Dog under light ether anesthesia; cannula in the pancreatic duct; *a*, carotid blood pressure; *b*, record of flow of pancreatic juice in drops. Time, twenty-five minutes. Tracing A: intravenous injection of 10 c.c. secretin (prepared fresh from dog's duodenal mucosa) at *x*. Tracing B: intravenous injection (at *x*) of 10 c.c. of the same secretin as in Tracing A, after being digested in normal human gastric juice at 37 C. for two hours.

TABLE 8.—SUMMARY OF TYPICAL EXPERIMENTS SHOWING THE ABSENCE OF SECRETIN IN "DUODENIN"

Dogs under ether anesthesia

Exp. No.	Number Duodenin Tablets Used	Secretion of Pancreatic Juice in Drops, Following Intravenous Injection					
		Control 10 c.c. Secretin	Duodenin in				Control 10 c.c. Secretin
			Distilled Water	0.4% HCl	70% Alcohol	0.9% NaCl	
1	3	29	0	0	0	1 (?)	28
1	6	..	..	1 (?)	..	..	..
2	18	16	..	6	..	..	16
3	5	14	..	0	0	0	8
3	25	...	..	1 (?)	..	..	..
4	100	110	..	0	..	..	67
5	150	19	..	0	..	0	8

facturers, "Duodenin (Armour) is recommended in the treatment of intestinal disorders where an increased flow of pancreatic, hepatic and intestinal secretion is desired. It is of specific value in proteid digestion on the theory that secretin and enterokinase stimulate the pancreas and activate its secretion."

We bought a quantity of Duodenin in the open market, and carried out on this product the same series of experiments as that used in the case of Secretogen. The results were similarly negative (Table 8).

In regard to both Secretogen and Duodenin, we assume that the manufacturers have tried to put secretin in them, but have been unable because they have failed, in all likelihood, to check their methods by physiologic standardization. These firms do not give any details as to the procedure they employed in their manufacture of secretin. Desiccated secretin of extreme potency has been prepared by various physiologists,[61] 1 mg. (1/64 grain) of which is active when given intravenously. It is difficult to conceive that any of these methods were used in the preparation of Secretogen or Duodenin.

CONCLUSIONS

1. Secretin is quickly destroyed by gastric juice and by trypsin.

2. Secretin is not absorbed in active form from the alimentary tract.

3. The presence of secretin or prosecretin cannot be demonstrated in the commercial preparations "Secretogen," "Elixir Secretogen" and "Duodenin" even when the therapeutic dose of the preparations is given intravenously. In the case of "Secretogen," intravenous injection of 100 times the therapeutic dose reveals occasionally an insignificant trace of secretin.

DISCUSSION OF RESULTS

It is, of course, objectionable that preparations containing no secretin should be advertised to the medical profession as containing this substance. The more important blunder, however, consists in the attempt to offer such preparations for oral administration, because even chemically pure secretin would be equally ineffective when taken by mouth. There is as yet no reliable evidence that lack of secretin is a primary or important factor in any disease. Even should this be established, secretin therapy, to be effective, must be intra-

61. Stepp (Note 13). Dale and Laidlow: Jour. Physiol., 1912, xliv, xi. Launoy and Ochslin: Compt. rend. Soc. de biol., 1913, lxxiv, 338.
62. Harrower: Practical Hormone Therapy, London, 1914, p. 70.

venous. Secretin has not yet been prepared in sufficiently pure state to render possible intravenous injection in man without injurious effects. And even when this has been attained, the very fleeting action of secretin will in all probability render secretin therapy as futile in all the diseases in which it is theoretically indicated as epinephrin therapy is in Addison's disease.

But there remains the alleged favorable effect from secretin therapy by mouth in various diseases in man. It is, perhaps, impertinent for laboratory men to comment on these clinical results. The ordinary "testimonials" need not be considered, but we should like to ask the serious worker who thinks he has actually obtained good results from secretin therapy how certain he is of the causal relation between the giving of secretin or alleged secretin and the abatement of the disease.

When a therapeutic measure not only lacks a positive basis in physiology and pathology but runs contrary to all the well-established experimental facts in these fundamental medical sciences, is it too much to ask that positive clinical findings be subjected to more than usual critical analysis before acceptance? *"Clinical tests,"* it is said, "covering a period of several years have proved that neither the condition in the stomach during digestion nor those in the intestine prevent the secretin from entering intact into the circulation." When we meet claims such as this, should we not scrutinize the "tests" as well as the men who make them?

We are indebted to Dr. J. H. Moorehead for assistance in part of the surgical work.

DELAYS IN PASSING ON PRODUCTS

Report of the Council on Pharmacy and Chemistry

The Council has adopted the following report and authorized its publication. W. A. PUCKNER, Secretary.

The Council frequently receives inquiries — some of them accompanied by expressions of impatience—concerning articles, reports on which appear to be delayed. It therefore seems advisable to make a statement of some of the factors which enter into this problem.

The Council fully realizes the importance of giving prompt information to the profession with regard to proprietary medicines under consideration. It therefore acts as soon as sufficient information is available to justify a definite judgment, and publishes its conclusions as soon as possible.

When adequate information is available at the outset, there is no delay in the publication of the Council's conclusions.

Unfortunately, but very naturally, there are many cases in which the information available at the time the product is submitted is not sufficient to justify the Council in coming to definite conclusions for or against the preparation. In some cases the manufacturer possesses the required information, but to obtain it from him takes time; in other cases the manufacturer does not possess the information—perhaps he did not realize the inadequacy of his evidence until the subject was brought to his attention by the Council.

Such cases might be dealt with in either one of two ways: The Council might at once reject the article because the claims for it are not supported by adequate evidence. Or, the Council might suspend judgment and give the manufacturer an opportunity to supply the information.

The first method — immediate rejection — would obviously be felt by manufacturers as a hardship. To afford the fullest possible opportunity for the presentation of the case, the Council follows the second method: that is, it suspends judgment and withholds publication of a report until reasonable time has been afforded for furnishing the required information, provided the manufacturer or agent appears to be making honest and diligent efforts to supply it. The collection and compilation of such information is sometimes a lengthy process, especially when the products are of foreign manufacture.

Although it would be easier for the Council to render an immediate decision than to assist manufacturers to supply the data necessary for the formation of an authoritative judgment, the Council cannot yield to importunities for hasty action. It must rely on the medical profession to bear in mind that the character of a product under consideration by the Council has not yet been determined. The Council holds that, during this stage, a product is suitable, at most, for experimental use.

INTRAVENIN P-H

Report of the Council on Pharmacy and Chemistry

The following report has been accepted by the Council and its publication authorized.

W. A. PUCKNER, Secretary.

Intravenin P-H (Intravenin Products Company, Inc., Philadelphia) is said to be

"An Alkaline Colloidal Compound of Ferrum, Calcium, Guaiacolum and Salicylates."

A more elaborate, but scarcely more informing, statement of composition is the following:

"The formula or more strictly the analysis for each 10 c.c. is:

"COLLOIDS

"Ferric Hydroxide	2.4 mg.
Hydrargyrum	.06 mg.
Guaiacolum Calcium	30 mg.

"IONS

"Calcium	8.5 mg.
Salicyl	52 mg.
Hydroxyl	7 mg.
Iodine	0.3 mg.
Sodium Chlorine	Indeterminate

"SALTS

"Sodium Chloride ..... 240 mg."

From these and similar befuddling statements it appears that Intravenin P-H is to be looked on as an alkaline sodium chlorid solution containing colloidal ferric hydroxid ("dialyzed iron"), a colloidal form of mercury, calcium guaiacolate, a salicylate and an iodid. It is therefore analogous to Bannerman's Intravenous Solution (THE JOURNAL A. M. A., Jan. 2, 1915, p. 70). As in the case of the Bannerman product, the claim that Intravenin P-H is composed of "official substances" is contradicted by the formula itself. This includes colloidal ferric hydroxid, colloidal mercury and calcium guaiacol, all unofficial substances. The formula is confusing and unsatisfactory, and thus essentially secret.

The properties of the substance are stated to be

"Alkaline, Anti-toxic, Anti-septic, Opsonic, Hemogenic, Anti-pyretic, Diaphoretic, Diuretic, Expectorant.

"Without Local or General Reaction or Contra-Indication."

It is recommended as

". . . now having marked success in the treatment of diabetes, incipient tuberculosis, neuritis, neurasthenia and various infections. Any resourceful physician will see many opportunities for its use."

The assertions advanced as grounds for the use of Intravenin P-H are unwarranted and in many instances false. For instance:

"Normal blood can accomplish almost anything in the human body — far better than subnormal blood reinforced by animal made serums, and on the other hand, abnormal blood is almost sure to cause some functional derangement or a series of derangements which further deteriorate its quality and make the way easy for bacterial invasion."

"The processes of nature are such that even simple and necessary elements like Calcium and iron are only absorbed from the alimentary tract when in certain organic combinations."

"Should the blood or the cells of the body lack calcium for instance and should it be administered in the form of a diffusible salt practically all would be excreted despite the need that existed. But if the patient were given a natural product containing calcium in a colloidal organic combination a fairly large proportion would be assimilated."

None of these statements is borne out by scientific evidence. Even if it were possible to admit the unfounded assertions of the company, the following facts would have to be considered:

Practically all of the conditions in which calcium and iron are usually administered are chronic disturbances, extending over long periods of time. The intravenous administration of drugs is too radical a procedure to be employed ad libitum in long-standing chronic complaints; it should be reserved for emergencies or acute conditions.

Intravenin P-H is not only an unscientific mixture but also essentially secret in composition. The claims made for it are exaggerated, misleading and false. The indiscriminate intravenous medication for which this preparation is offered may result in serious harm. The Council voted that the preparation be declared ineligible for New and Nonofficial Remedies and that this report be published.

LECITHIN PREPARATIONS OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report was sent to the manufacturers of the various lecithin preparations mentioned therein. As the replies of the manufacturers were obviously written from the commercial point of view and did not affect the Council's conclusion that lecithin, when indicated, would be given more advantageously in the form of yolk of egg than in the less pure manufactured product, the Council directed that the report be published, together with extracts from the replies of the manufacturers.

W. A. PUCKNER, Secretary.

Commercial lecithin preparations are at best very impure substances; all are more or less altered from the original composition. Even with great care, the methods of extraction and drying always produce considerable decomposition; and in some cases the phosphorus and nitrogen contents bear but little relation to the theoretical values. (Long, J. H.: *Jour. Am. Chem. Soc.,* xxx, 881. McLean, Hugh: *Chem.*

Abstracts, May 20, 1915). There is not the slightest reliable evidence that commercial lecithin has any advantage over the lecithin contained in natural foods; the weight of probability is on the other side.

The doses recommended, moreover, are absurdly small; and the amount thus administered is without practical value. Why administer a few milligrams of a more or less decomposed lecithin when it is possible to give a far larger weight of a purer substance in the form of yolk of egg?

In view of these considerations the Council voted that the following proprietary products be omitted from the next edition of N. N. R.:

Glycerole of Lecithin
Lecibrin
Lecithin Solution
Lecithol
Neuro-Lecithin-Abbott

and that the general article on "Lecithin Preparations" be transferred to the annual Council Reports as a matter of record.

The report was submitted to the manufacturers. Their replies were evidently based on commercial considerations, and called for no modification in the report.

The referee recommended that the preceding report be published together with the following extracts from the replies of the manufacturers:

From Armour and Company:

"We are selling a good deal of Lecithol and it seems to be giving satisfactory results in some quarters. . . . We shall continue to advertise Lecithol along the lines we have employed heretofore."

From the Abbott Laboratories:

"We can assure you of our confidence in the therapeutic value of Neuro-Lecithin. This has been attested by reports of favorable results sent us by many physicians, as well as by the periodical literature of the last few years which contains a considerable number of very encouraging references to lecithin therapy."

From Fairchild Bros. & Foster:

"We would like simply to say that the physician and the Council must be aware of the circumstances and the purposes which actuated us in placing lecithin at disposal, viz., the studies—research—of lecithin and the properties attributed to it and which led to inquiry for and consideration of it. The *quantities* proposed for medicinal use were not suggested by us; the suggestion of lecithin in small quantities as a therapeutic agent was obviously directed by those who proposed it. . . . The question whether lecithin, per se, has therapeutic properties in contrast to lecithin as naturally contained in food substances, is something we do not undertake to decide. The Council, on purely theoretical grounds, decides in the negative notwithstanding clinical

experience — internal and hypodermic — and thus would deny lecithin the status of a new and nonofficial remedy, worthy of at least tentative progressive clinical consideration. We can only say that we offered bona fide lecithin and that we did not make the investigation of lecithin a pretext for the sale of all sorts of lecithin 'jumbles' with lecithin in small proportions, taking their name and making their bid on lecithin."

Below appears the general article which has been omitted from N. N. R.:

Lecithin Preparations

Lecithins are fat-like bodies belonging to the group of phosphatides. They all consist of glyceryl esters containing two fatty acid radicals and the phosphoric acid radical in which one of the residual hydrogens is replaced by the choline group. The fatty acid may be palmitic, oleic or stearic and various combinations are known to exist; for example, distearyl lecithin, stearyl palmityl lecithin and so on. The commercial lecithins usually include the closely related kephalins.

On saponification the lecithins split more or less readily into choline, the fatty acids and glycerophosphoric acid, and by fusion with alkali nitrate and carbonate they yield alkali phosphate. They occur, free or in combination as lecithoproteins, most abundantly in certain animal tissues, but there are also vegetable lecithins. The lecithins of commerce are obtained usually from yolks of eggs or from calves' or sheep's brains.

Numerous processes have been devised for the preparation of lecithin from egg-yolk or animal tissue. From egg-yolk it may be obtained by making an alcoholic extract and precipitating by cadmium chloride. The precipitate is washed with alcohol and ether, mixed with 80 per cent. alcohol and warmed with the proper amount of ammonium carbonate to remove the cadmium. After filtering hot and concentrating the filtrate the lecithin is thrown down by cooling to a low temperature—10 C. or below. The precipitate is taken up in chloroform and reprecipitated by acetone.

From tissues it is obtained by extracting with warm alcohol and ether, concentrating the extract, precipitating with acetone and repeating the operations.

Pure lecithin is white, but the commercial preparations are yellowish-brown wax-like solids, which are not soluble in water but form milky emulsions which exhibit the myeline figures under the microscope. The solubility in cold alcohol or ether is slight, but heat aids it. Lecithins are not soluble

in acetone. They are hygroscopic and the water mixtures undergo decomposition on standing. They darken on exposure to air and light.

The alcoholic solution is precipitated by platinum or cadmium chloride. It is decomposed by alkalies with the formation of choline and trimethylamine. The ash contains phosphoric acid. The different lecithins contain from 3,84 to 4.12 per cent. of phosphorus and 1.73 to 1.86 per cent. of nitrogen. The ratio of nitrogen to phosphorus should be at 1 to 2.21.

Lecithin is incompatible with alkalies; it should be kept in well-stoppered bottles and should be protected from the light.

The content of lecithin (plus kephalin) in tissues is about as follows:

	Per Cent.
Egg-yolk	8 to 12
Egg-white	0.1 to 0.2
Liver	2.0 to 3.0
Kidney	2.0 to 3.6
Lung	2.0 to 3.0
Pancreas	2.0 to 3.0

Actions and Uses.—The lecithin preparations have been recommended in many pathologic conditions, especially in malnutrition and sexual debility. Moderate doses are said to bring about a marked retention of nitrogen and phosphorus, but satisfactory proof of this is lacking. It is extremely unlikely that the small doses which have been recommended in pill or tablet form or in emulsions can have anv perceptible action, in view of the fact that many of our natural foods contain much greater weights of available lecithins than the medicinal doses provide. There is no good basis for the statement that the free lecithin has a greater food value or is more readily assimilated than is the substance as found in eggs or tissue. The reverse proposition is much more likely to be true, especially when it is considered that the commercial preparations are usually somewhat altered or decomposed in the process of separation.

Dosage.—Given by the mouth in the form of pills, tablets or glycero-alcoholic emulsions. The amount of actual lecithin ingested in this way is usually small because of the doubtful purity of the original preparation. Several doses, as commonly administered, would be required to furnish the amount of lecithin present in a small egg.

PANTOPON ROCHE (PANTORIUM HYDROCHLORICUM) ACCEPTED FOR N. N. N.

Report of the Council on Pharmacy and Chemistry

The following report has been accepted by the Council and its publication authorized.

W. A. PUCKNER, Secretary.

Pantopon Roche (Pantopium Hydrochloricum), manufactured by F. Hoffmann LaRoche and Company, Basel, Switzerland (The Hoffmann-LaRoche Chemical Works, New York), is a mixture of the hydrochlorids of the alkaloids of opium in the proportion in which they exist in Smyrna opium, containing 50 per cent. of anhydrous morphin hydrochlorid.

When pantopon Roche (pantopium hydrochloricum) was first brought to the attention of the Council, the claims conveyed the impression that it was free from the undesirable side actions of opium, that it was much safer, and that it could be used in a great variety of conditions in which physicians would hesitate to employ opium as such. At that time the Council held that the name did not sufficiently protect the public against the habit-forming and other dangers inherent in such mixtures. The Hoffmann-LaRoche Chemical Works having refused to adopt a more descriptive name, the Council, without considering other objections, held pantopon ineligible for New and Nonofficial Remedies.[1]

The manufacturers later requested a second consideration. At this time they agreed to change the name of their product to Pantopium. The Council, however, was forced to reject the preparation because of the claims made for it, though these were less sweeping than at first.

Now the claims for pantopon have been reduced in such a way that they may be accepted. They are:

Pantopon contains the alkaloids of opium, and has the same advantages over morphin that opium is believed by some to possess. Being free from opium extractives, it has the advantage over opium and opium extracts in that it may be given hypodermically.

The manufacturers have consistently emphasized the morphin content of pantopon; there seems now to be no danger

1. See Pantopon Rejected, THE JOURNAL A. M. A., April 29, 1911, p. 1278.

that this will be overlooked by the prescriber. Also, to guard against all possibility of such danger, the manufacturers announce their intention of invariably using the synonym "pantopium hydrochloricum" in connection with the name "pantopon." Moreover, the operation of the Harrison law has greatly lessened the danger of indiscriminate and thoughtless use of narcotics.

In view of all these considerations, therefore, the Council has waived its objection to the name, and, on the basis of the moderate therapeutic claims now made, has accepted pantopon Roche (pantopium hydrochloricum) for inclusion with New and Nonofficial Remedies.

PROPRIETARY NAMES FOR LIQUID PETROLATUM

Report of the Council on Pharmacy and Chemistry

The Council has accepted the following report and authorized its publication.

W. A. PUCKNER, Secretary.

A former report of the Council (Liquid Petrolatum or "Russian Mineral Oil," Report Council Pharm. and Chem., THE JOURNAL, May 30, 1914, p. 1740) called attention to the large number of concerns that were placing on the market liquid petrolatum as a proprietary under coined names. Since then the number of such products has increased. The Council has been requested by several concerns to consider their products put out under proprietary brand names.

The rules of the Council affirm that "the application of 'trade names' to official or established nonproprietary substances tends to confusion and fosters many abuses." In accordance with this general ruling, the Council has invariably refused to countenance proprietary names applied to liquid petrolatum. The Council holds that proprietary or coined names for this substance are detrimental to medical progress, since they are sure to foster the impression that the particular product is different from liquid petrolatum. Manufacturers have been advised that there is no objection to distinguishing their products by the addition of their firm name or the initial representing the firm name; for instance, "Liquid Petrolatum, A. B. and Co." or "Liquid Petrolatum, Smith." The Council also believes that such designations as "Star Liquid Petrolatum" or "Liquid Petrolatum, Anchor Brand," may be regarded as unobjectionable, provided that the words "Liquid Petrolatum" are always used in connection with the brand designation and given equal prominence.

RADELIUM AND RADELIUM GENERATOR

Report of the Council on Pharmacy and Chemistry

The Council has accepted the following report and authorized its publication.

W. A. PUCKNER, Secretary.

Radelium and the Radelium Generator are marketed by the Radio-Active Water Company, Portland, Ore. The company which wished to advertise its preparation and device in THE JOURNAL of the American Medical Association, was informed that the article must first be passed on by the Council on Pharmacy and Chemistry. The preparation was therefore submitted to the Council.

Radelium is said to be "an insoluble radium salt," the identity of which "is the manufacturer's secret." It is marketed solely as the essential component in the Radelium Generator, an apparatus for preparing radioactive drinking water. This generator consists of a porous clay cylinder said to contain "Radelium," which is fixed in a silver-plated metal bottle with a screw top carrying a stopcock. It was not possible to determine the actual amount of radium in the porous clay cylinder, because the contents of the cylinder were not accessible for direct examination, and the apparatus was not to be damaged. The radioactive efficiency of the device, however, could be ascertained by determining the emanation in the water. The Council's radium referee found that, used according to the printed instructions, the Radelium Generator imparted to 194 c.c. of water stored in it for twelve hours, 0.082 microcurie of radium emanation. This is the amount that would be produced by 0.96 microgram of radium element in this length of time, if all of the emanation produced were transferred to and dissolved in the water. The amount of radium contained in the clay cylinder undoubtedly was greater than that mentioned above, but how much greater is of no practical importance, since any estimate of the therapeutic value of the apparatus must be based on the activity of the water to which the emanation is imparted.

The amount of emanation contained in the water is much smaller than the ordinary therapeutic doses now employed. The water, while far weaker than the radioactive water produced by other generators available, is more active than natural radioactive water; this, however, has no therapeutic significance, for the therapeutic value of natural radioactive water is still an open question, concerning which authorities differ. The natural waters cannot be taken as a standard,

since their value is problematical. The circular, nevertheless, conveys the impression that the efficacy of radioactive waters in many diseases has been proved beyond a doubt. For instance:

"The waters in hundreds of the world's most famous natural springs have an inherited reputation for possessing curative powers. Modern scientific research has established beyond a shadow of a doubt that it is the radium emanation that, above all things, is the curative agent and disease destroyer."

As for the preparation itself:

"Radelium is a remedy of great value in the treatment of all forms of Rheumatism, Gout, Neuralgia, Sciatica, Catarrh of Mucous Membrane and Uterine Catarrh, Dyspepsia, Scrofula, Menstrual Disorders, Arteriosclerosis and Skin Diseases."

The evidence presented in support of these extensive claims includes "Statements from Those Who Have Used Radelium." The writers of these testimonials are laymen and the evidence is worthless. The following are fair illustrations:

"Suffering from a nervous breakdown, I became a mental and physical wreck. . . . After using Radelium for three weeks, I . . . could sleep, eat, think and rest . . . and now (3 months) I am practically a well man, rapidly gaining vitality. It did wonders for me."

"It has kept my blood in good condition and stopped the nervous spells I used to have."

"My stomach has troubled me for about a year and a half, and just before I started to take Radelium, I was in poor health, and very, very nervous, but at present I feel perfectly well."

The fact that the identity of Radelium is kept secret is a conflict with Rule 1 which is particularly objectionable in view of the imperfect knowledge of radium producing preparations; the unwarranted and exaggerated therapeutic claims made for it constitute a conflict with Rule 6, and the character of the advertising propaganda, which invites the indiscriminate use by the public of a therapeutic measure still in the experimental stage, constitutes a conflict with Rule 4. The Council directed that Radelium and the apparatus said to contain it be refused recognition.

SENG

Report of the Council on Pharmacy and Chemistry

The Council has adopted the following report and authorized its publication.

W. A. PUCKNER, Secretary.

Seng (Sultan Drug Co., St. Louis) is called by the manufacturers:

". . . a palatable preparation of Panax (Ginseng) in an aromatic vehicle."

Regarding ginseng *(Panax quinquefolia)* the United States Dispensatory, nineteenth edition, page 1603, says:

"The extraordinary medicinal virtues formerly ascribed to ginseng had no other existence than in the imagination of the Chinese. It is little more than a demulcent, and in this country is not employed as a medicine."

No discussion of ginseng is to be found in the more recently published books on pharmacology, materia medica and therapeutics, evidently because their authors agree with this estimate.

On the other hand, physicians are told through the medium of advertisements appearing in medical journals that Seng is:

"An efficient remedy in all affections in which the gastro-intestinal glands need stimulating.

"Exceptionally useful in atonic indigestion, malnutrition, convalescence from the acute diseases, and all digestive disorders characterized by deranged or depressed functions." (*Woman's Medical Journal*, July, 1914.)

According to the label, Seng is indicated in "indigestion," "malassimilation," "malnutrition" and "wasting diseases." It is also stated—though the preparation is admitted to contain 18 per cent. of alcohol—that to give babies "ten to fifteen drops in water or milk during feeding" is a proper procedure and that "For Colic, Flatulency, etc., the dose for an adult or child may be repeated every half hour until relieved."

The following are some of the exaggerated therapeutic claims made for this preparation of a worthless drug:

"As a result of its administration the gastro-intestinal secretions are augmented, the digestion of food is substantially increased, and fermentative processes are promptly overcome."

"Seng will specifically encourage the secretion of the juices in the entire alimentary tract . . ."

The formula furnished for Seng is non-quantitative and therefore meaningless. The preparation is exploited in a manner to encourage its ill-advised use by the public, and exaggerated and unwarranted therapeutic claims are made for it. The use of an inefficient or worthless drug like ginseng, moreover, is detrimental to rational therapeutics. The Council therefore voted that Seng be refused recognition for conflict with Rules 1, 4, 6 and 10.

ABSTRACTS OF COUNCIL ACTION

Reports of the Council on Pharmacy and Chemistry

The Council has authorized the following brief statement of its consideration during the current year of certain articles which were not deemed to require an extensive discussion. (See preface to this volume.)

G. G. Phenoleum Disinfectant

(From The Journal A. M. A., Jan. 30, 1915, p. 456)

This material is a solution sold by the G. G. Chemical Company, Inc., of New York and claimed to be composed of the following ingredients:

". . . Volatile Hydrocarbons, Phenols, Resin Acids, Sodium Oxide and Heavy Hydrocarbons."

For it they claim the following properties:

"PREVENTS DISEASES, KILLS SEWER GAS, PURIFIES THE TOILET."

"For any skin disease, 'tis as good for man as for beast."

As to its virtues as a disinfectant the manufacturers claim a phenol coefficient of 5 or 6. The disinfecting power is not however stated on the label as required by the Council for phenol disinfectants. Disregarding entirely the fact that disinfectants are available with a much higher phenol coefficient than the one claimed for this product, the statement is made that it is

". . . the most powerful disinfectant known."

As such claims are self-evidently unwarranted, G. G. Phenoleum Disinfectant was refused recognition.

Phytin and Fortossan

(From The Journal A. M. A., Jan. 30, 1915, p. 456)

Phytin, manufactured by the Society of Chemical Industry, Basle, Switzerland, and sold by A. Klipstein and Co., is an organic phosphorus compound said to be the "Acid Calcium-Magnesium Salt of Phytinic Acid (Inosit Phosphoric Acid or Anhydro-Oxymethylene-Diphosphoric Acid)" obtained from cereals and legumes.

The trade package of Phytin constitutes an indirect advertisement to the public.

The Council rejected Phytin because unwarranted and exaggerated therapeutic claims are made for this product based on the entirely undemonstrated assumptions: (1) that phosphorus is assimilated only from organic combinations (it is even implied that this must be in the form of Phytin, and that milk is incapable of supplying the phosphorus needs of infants); (2) that a long list of diseases, ranging from rickets to hysteria, are due to deranged phosphorus metab-

olism; (3) that all these diseases are cured or markedly benefited by Phytin.

In brief, the claims rehearse every point of the more or less discredited phosphorus propaganda, in exactly the same way as it was rehearsed successively by the exploiters of hypophosphites, lecithin, glycerophosphates, and amorphous phosphorus. It is conceded by the writers of the advertising pamphlets for Phytin that the preceding claims were erroneous; but no evidence is given to warrant the belief that the Phytin claims are less erroneous.

The misleading statements are most extreme. By the use of bold type particular stress is laid on the preposterous and vicious claim that Phyytin

"radically and permanently removes sexual debility."

Fortossan is a preparation of Phytin and sugar of milk, also manufactured by the Society of Chemical Industry, Basel, Switzerland, and sold by A. Klipstein and Co. Since Fortossan is a simple preparation of Phytin the Council voted that the rejection of Phytin should also apply to Fortossan.

Virol

(From The Journal A. M. A., Feb. 20, 1915, p. 683)

Virol, sold in the United States by the Etna Chemical Company, is put out by Virol, Ltd., London, England. It is said to be

"A preparation of bone marrow, red bone marrow of medullary structure of ox rib and calf bones, eggs, malt extract, and lemon syrup made from fresh fruit."

"Marrow fat is emulsified with extract of malt, lemon syrup and eggs, it is further enriched with soluble phosphates of lime, iron and soda, and glycerine solution of red bone marrow."

Many of the therapeutic claims made for Virol the Council considered grossly exaggerated; among them are the following:

". . . a complete food for children."

". . . a complete nutrient."

"The value of the Lime-Salts (representing the Egg Shells) contained in Virol is fully illustrated in its influence upon Rickets; whilst Struma, Chronic Bronchitis, Anaemia and Influenza are all combated by its use in a degree, which, we venture to say, has never been approached."

"The fat, as represented by the Marrow-bone and Egg Yolk, is so minutely divided that it admits of even far more rapid absorption by the *villi* of the intestine than milk."

"It is an ideal form of food, readily digested and assimilated in the weakest of conditions."

"Virol has a marked effect on the metabolism of the body, increasing the production of opsonins and stimulating phagocytosis. As an adjuvant to the natural defensive processes of the patient in all diseases of bacterial origin its value can scarcely be over-estimated."

The objections of the Council were transmitted to Virol, Ltd. The firm's reply was reported to the Council by the

referee of the Committee on Therapeutics who held that no adequate or satisfactory answer had been made to the objections raised against the advertising claims for Virol.

The claims made for Virol being unsubstantiated and unwarranted, the Council voted that the preparation be refused recognition.

In accordance with the practice of the Council, the exploiters of Virol were afforded an opportunity to comment on the foregoing statement before its publication. On their objecting to the findings, the entire matter was turned over to a second referee. This referee, in making his report, reviewed the claims made for Virol and commented on the lack of evidence to substantiate these claims. He stated that a chemical analysis of the preparation had yielded the following result:

"Sugar, as maltose	60.0 per cent.
"Fat	13.2 per cent.
"Proteins	3.2 per cent.
"Ash	1.6 per cent.
"Water and volatile matter	21.6 per cent.

"There is no appreciable diastatic action. A little glycerol is present in the volatile matter. The preparation is therefore an extract of malt with fat and a small amount of protein."

He then continues:

"That Virol has food value cannot be denied, but that it has sufficient value to warrant the claims of the manufacturers is not evident. Virol cannot be considered a complete food, as the advertising literature reiterates, or an ideal food for infants. The amount of protein is far too low in comparison with the carbohydrates to warrant this view. The dosage recommended is not large. Thirty gm. a day would furnish only about 1 gm. of protein and 4 gm. of fat. The 3 teaspoonfuls a day recommended for children would furnish protein and fat even below this.

"If employed alone it cannot be a complete or sufficient food, and if employed along with other articles of diet—milk and bread, for example—it is not easy to see wherein lies the efficacy of the small weights of fat and protein added in the form of Virol. Here the demand made on our credulity is too great, as the protein in the preparation is the familiar protein of eggs, meat and malt, and the fat largely that from the egg-yolk and marrow, according to the claims. It is not known that any specific virtues reside in these bodies, or in the egg-shells, also claimed as present.

"In the opinion of the present referee there is nothing in the composition of Virol to iustify the claims made for it.

The judgment and recommendations of the first referee follow from the facts and must be accepted by the Council."

The Council directed that the previously prepared report be allowed to stand and that it be published along with a suitable reference to the report of the second referee.—

Salesthyl and Sal-Hyl

(From The Journal A. M. A., Feb. 20, 1915, p. 684)

Salesthyl and Sal-Hyl, two preparations exploited by the New York Salesthyl Corporation, were submitted to the Council for inclusion in New and Nonofficial Remedies. Salesthyl, a liquid, marketed in capsules, was stated to be the menthyl ester of methyl salicylate. Sal-Hyl was said to be an ointment of Salesthyl, and its exact composition was not disclosed.

The first preparation, Salesthyl, is claimed to have the ordinary therapeutic actions of salicylates in general. The specific advantages appertaining to this product however, according to the manufacturers, make it more efficient; for example, they say it is "free from toxic effects," "a resorbent of uric acid" a "bacterizer" with "never-failing results."

From either a chemical or a pharmacologic standpoint, it is difficult to understand how the menthyl ester of methyl salicylate could be at the same time more efficient and less toxic than methyl salicylate itself. As to the peculiar terms "bacterizer" and "resorbent of uric acid," the meaning of which must be gessed at, the manufacturers have submitted no evidence that their products possess these hitherto unknown virtues.

The claims as to non-toxicity and greater efficiency were supported in the advertising circular by tabulated reports said to have emanated from "well-known medical practitioners," who for the most part were asserted to be connected with New York hospitals. All of these reports were dated July, 1912. Investigation showed that these reports must have been written within two months after these "well-known practitioners" had graduated from a homeopathic school. This school claims no special experience with salicylates (in fact the use of salicylates in rheumatic conditions is not considered a homeopathic measure). The Council held it misleading to characterize these recent graduates as "well-known practitioners." The reports themselves, however, were insufficient and unconvincing and even contradicted the claimed superiority of Salesthyl.

The Council also objected to the name "Salesthyl" as likely to be confused with the well-established name

"sal-ethyl," a salicyl ester described in New and Nonofficial Remedies.

The false claims having been brought to the attention of the present owners—the New York Salesthyl Corporation—they explain that they obtained the reports among the assets of their predecessors, the "American Salesthyl Corporation"; that they acted in good faith; that they will withdraw the pamphlets from circulation; and that they desire to make all needed reforms. In view of this the Council voted that Salesthyl and Sal-Hyl be refused recognition with the understanding that further consideration will be given the products when the needed reforms have been made and satisfactory evidence of the value of the products has been submitted.

Analutos and Analutos Tablets

(From The Journal A. M. A., Feb. 20, 1915, p. 684)

Analutos and Analutos Tablets, 0.5 Gm. were submitted to the Council by D. A. Zwigtman, Niles, Mich., representing the Royal Pharmaceutical Works of Meppel, Holland.

Analutos was stated to be the calcium salt of acetyl-salicylic acid. The advantages claimed over acetyl-salicylic acid itself are that Analutos is more soluble and less liable to produce gastric disturbance. The evidence submitted was not sufficient to show that Analutos has any advantages over acetyl-salicylic acid, or that it or its properties were discovered by the manufacturers. It is simply an unessential modification of a well-known substance, offered without evidence of superiority or originality. The Council held that physicians should not be burdened with a new, arbitrary name which does not even indicate the relation of the product to its well-known basic constituent. Accordingly it was voted that Analutos and Analutos Tablets be refused recognition.

Budwell's Emulsion of Cod-Liver Oil, Nos. 1 and 2

(From The Journal A. M. A., Feb. 20, 1915, p. 684)

The Budwell Pharmacal Company, Lynchburg, Virginia, which markets these preparations, claims that "No. 1" contains cod-liver oil, "Iodide of Arsenic," "Iodide of Calcium," and "Iodide of Manganese." "No. 2" is said to contain in addition to the ingredients of No. 1, creosote carbonate and guaiacol.

It is known that arsenous iodid is decomposed by contact with water. It is recognized that creosote carbonate is unstable and prone to liberate creosote. Iodide of manganese not being official, the supply on the market is not controlled

in any way: tests of purity are not prescribed by the Pharmacopeia, the National Formulary, New and Nonofficial Remedies or other books of standards. Therefore doubt must be expressed as to the accuracy of the formulas as given. The Council cannot accept such statements of composition without further evidence.

"No. 1" is commended for use in

"Chronic Rheumatism, Glandular Swellings, later forms of Syphilis, convalescence from Scarlet Fever, La Grippe and Malaria, Chronic Malarial Infection, Marasmus, Joint or other suppuration of standing, diseases of skin, chorea, anaemia, neurasthenia, obstinate neuralgia, scrofulous affections in general, and diarrhoea or dysentery (sub-acute or chronic) in childhood."

"No. 2" is said to be

"Prepared especially for the treatment of Chronic Throat, Nasal, Bronchial and Pulmonary Diseases."

In the advertising circular statements regarding the various ingredients of Budwell's Emulsion are quoted from obsolete text-books. These statements, for the most part, do not represent modern opinions on the subject. For instance, the circular praises the action of guaiacol as eliminated directly by the lungs, thus exerting a beneficial local effect and causing bacilli to diminish in numbers or to disappear. All of this is directly contradicted in authoritative modern publications on pharmacology, which hold that the excretion of guaiacol by the lungs is infinitesimal and its action on bacilli is nil. The Council held the preparations in conflict with its rules as follows:

1. Many of the therapeutic claims are exaggerations.

2. The method of exploitation amounts to an indirect invitation to the public to use these preparations as "consumption cures."

3. The preparations are unscientific, they constitute a reprehensible invitation to uncritical prescribing and their use is inimical to the best interests of the profession and the public. It is difficult to imagine in what conditions such a combination would be indicated. These preparations are a remnant of the days of polypharmacy. Their use is not in keeping with present medical thought and practice.

Colchi-Sal

(From The Journal A. M. A., March 20, 1915, p. 1016)

Colchi-Sal, said to be made by the Anglo-American Pharmaceutical Co., Ltd., New York, is advertised, sold and "guaranteed" (sic) by E. Fougera and Co., Inc., New York. According to the label of a recently purchased specimen:

"Each Capsule contains Cannabis Indica (Active Principle of) 1-500th Grain (⅛ Milligram); Colchicine (Crystallized) 1-250th Grain (¼ Milligram); Methyl Salicylate 20 Centigrams."

The advertising circular around the bottle adds that the mixture also contains "appropriate aromatic adjuvants."

It is recommended in "Gouty and Chronic Rheumatic Manifestations," "acute cases of Gout," "intestinal auto-intoxication or dyspepsia," "bilious headaches," etc. Salicylates are generally recognized as valuable in acute manifestations of acute articular rheumatism; colchicum is useless in these conditions. Both salicylates and colchicum are practically useless in chronic rheumatic and in chronic gouty affections. For dyspepsia, bilious headache, etc., salicylates are distinctly contra-indicated and the drastic purgation produced by colchicum would not be thought desirable. Though methyl salicylate administered internally is not generally considered so efficient as sodium salicylate, it is asserted that it

". . . is found far more effective than salicylate of soda or other salicylic derivatives when given in conjunction with colchicine as Colchi-Sal."

Further, the highly improbable and unsubstantiated claim is made that "the active principle of *Cannabis indica*" (whatever that may be) "corrects any tendency of the colchicine to irritate the gastro-intestinal tract" and that the "appropriate aromatic adjuvants" "prevent intolerance of the methyl salicylate."

Colchi-Sal is put up in a way to appeal to the public; the bottle has the name "Colchi-Sal" blown in the glass; the label gives full instruction for the use of Colchi-Sal, and also the price, suggesting that the preparation may be freely purchased. Wrapped around the bottle is a circular advising its use in various affections.

The physician who acts on the advice that it is well to "insist on the pharmacist dispensing original bottles . . ." of the "little green capsules" actually suggests to his patient the use of this preparation of methyl salicylate and colchicum in conditions in which these drugs may do much harm and in which proper treatment is imperative.

Colchi-Sal is typical of unscientific ready-to-take proprietaries. It was held ineligible for New and Nonofficial Remedies because of its secret composition, viz., the unknown nature of the "active principle of Cannabis indica" (Rule 1); because the circular in the package and the name blown in the bottle constitute advertisement to the laity (Rule 4); because the claim that cannabis indica removes the gastro-intestinal irritation, and the claim of the superiority of methyl salicylate are unwarranted therapeutic claims (Rule 6); because the name does not indicate the presence of the habit-forming cannabis indica, and because of its unscientific composition (Rule 10).

Waterbury's Compound

(From The Journal A. M. A., March 20, 1915, p. 1016)

The Waterbury Chemical Company having requested that the Council reconsider its action of four years ago (see THE JOURNAL A. M. A., Oct. 9, 1909, p. 1201) on the product then known as Waterbury's Cod-Liver Oil Compound, now called Waterbury's Compound, the matter was submitted to a referee. The referee reported that the statement now made as to the composition of this product is as follows:

"Made from Cod Liver Oil, Digestive Ferments, Malt Extract Unfermented, Hypophosphites Comp. Special, Ext. Cherry, Eucalyptus, Aromatics, etc."

He held that the Waterbury Chemical Company has not submitted satisfactory evidence to indicate that the objections of the Council's former unfavorable report have been met; that there is no evidence that the product is a substitute for cod-liver oil in any way; and that under the present methods of exploitation it constitutes what is at least an inferential fraud; and recommended that no further consideration be given to Waterbury's Compound. The report was adopted by the Council.

Hagee's Cordial of the Extract of Cod Liver Oil Compound

(From The Journal A. M. A., April 10, 1915, p. 1262)

This is one of the "oilless" cod liver cordials. Like other manufacturers of such extracts, the Katharmon Chemical Company, St. Louis, which owns Hagee's Cordial, attempts to trade on the reputation long enjoyed by cod liver oil as a promoter of growth and nutrition. The following is the statement of composition furnished by the company:

"Each fluid ounce of Hagee's Cordial of the Extract of Cod Liver Oil Compound represents the extract obtainable from ⅓ fluid ounce of Cod Liver Oil (the fatty portion being eliminated), 6 grs. Calcium Hypophosphite, 3 grs. Sodium Hypophosphite, ½ gr. Salicylic Acid (made from Oil Wintergreen), with Glycerin and Aromatics."

And here are some of the therapeutic claims:

"Tonic, Stimulant, Alterative, Reconstructive, Nutritive and Digestive."

"Useful in phthisis pulmonalis, scrofula and all chronic pectoral complaints, coughs, colds, brain exhaustion, nervous debility, palsy, chronic cutaneous eruptions and impaired digestion."

Of course, these absurd claims hark back to the time of the prevalence of the now discarded theory that the valuable properties of cod liver oil reside, not in the fat, but in certain nitrogenous, alkaloid-like constituents present in infinitesimal amounts. Further "playing up" this theory:

"The prescriber may know that in our preparation he is getting, in easily assimilable and palatable form, the very properties that make cod liver oil the best of reconstructives.

"When you prescribe cod liver oil you are after the active principles —why not give the active principles themselves."

Proprietary manufacturers usually ignore scientific investigations which establish facts adverse to proprietary claims; but the same proprietary manufacturers are quick to seize on any theory that can be twisted into support of their interests. Thus, recent investigations having shown that cod liver oil, like butter and egg yolk fat, possesses certain growth-promoting properties not found in some other fats, the promoters of Hagee's Cordial claim these properties of cod liver oil for their extract. They assert:

"Recent Chemical Investigations of Cod Liver Oil show that the active principles contain the nutritive qualities attributed to the whole oil."

The Council has previously expressed the opinion[1] that the preponderance of evidence indicates that whatever therapeutic value cod liver oil may have depends chiefly, if not entirely, on its fat (oil). There never was any evidence or scientific authority for the theory that the therapeutic value of cod liver oil was independent of its fat content. The fact that the fat is the growth-promoting element has already been shown, and J. P. Street, chemist for the Connecticut Agricultural Experiment Station (THE JOURNAL A. M. A., Feb. 20, 1915, p. 638), in a series of experiments on a number of the so-called extracts of cod liver or cod liver oil (including Hagee's Cordial) has conclusively demonstrated that the growth-promoting properties of the oil are not to be found in the extracts. Street placed rats on a ration not sufficient to maintain normal nutrition and growth for an extended period. After the rats had been on this ration for some time and a failure to maintain weight was indicated, an amount of dealcoholized Hagee's Cordial was substituted for a portion of the lard contained in the ration. Later Hagee's Cordial was replaced by cod liver oil.

Street says:

"None of the four rats did well on Hagee's Cordial; in fact, they lost 1.2 to 15.4 gm. during feeding periods of from seven to fourteen days."

"The rats failed so quickly when put on Hagee's Cordial that in two cases the animals did not recover even when put on the full cod liver oil ration."

". . . the four rats during the Hagee period, instead of gaining the normal 24 gm., actually lost 36.2 gm., while during the cod liver oil period instead of gaining 114 gm., they gained 156.4 gm."

"The inferiority of Hagee's Cordial as a reconstructive and a nutrient compared with ordinary cod liver oil is apparent."

Hagee's Cordial of the Extract of Cod Liver Oil Compound has neither the nutritive qualities nor the reconstruc-

1. THE JOURNAL A. M. A., Oct. 9, 1909, p. 1201.

tive efficacy of cod liver oil. This mixture is worthless for the conditions for which it is advertised, and is marketed under misleading and unwarranted claims. It is recommended that Hagee's Cordial be held ineligible for New and Nonofficial Remedies.

Wampole's Perfected and Tasteless Preparation of an Extract of Cod Liver

(*From The Journal A. M. A., April 10, 1915, p. 1262*)

Wampole's Preparation is another of the oil-free "extracts" of cod liver. The following formula (which, be it observed, is non-quantitative and therefore practically worthless) is published by the owners, Henry K. Wampole & Co., Inc.:

"Contains a solution of an extractive obtainable from fresh cod livers, the oily or fatty portion being afterward eliminated. This extractive is combined with Liquid Extract of Malt, Fluid Extract of Wild Cherry and Compound Syrup of Hypophosphites (containing Calcium, Sodium, Potassium, Iron, Manganese, Quinin and Strychnin)."

An alcohol content of 17 per cent. is declared on the label. The following claims are typical of those made for the preparation:

"This grease, or oil, is not present in Wampole's Preparation of the Extract, which *is palatable* and, at the same time, very efficient as a stimulant to the centers of nutrition and assimilation. It is unsurpassed as a reconstructive tonic . . ."

"[Cases] with a marked tendency to pulmonary troubles, . . . if a timely impulse be given them, will easily shake off the impending evil. Wampole's Preparation gives the timely impulse . . ."

In the Council's opinion, as previously expressed,[1] such therapeutic value as there may be in cod liver oil is chiefly, if not altogether, due to the fat (oil). Lately, the investigations of J. P. Street of the Connecticut Agricultural Experiment Station have definitely disproved the claims made for the Wampole's and similar preparations. In Street's experiments, rats were placed on a ration insufficient for normal nutrition and growth. After the rats had been on the ration for a time long enough for inability to maintain weight to become evident, dealcoholized Wampole preparation was substituted for a portion of the lard contained in the ration. Later the Wampole preparation was replaced by cod liver oil. From these experiments it appears that, although the Wampole preparation is said to contain malt extract and sugar, it does not show the advantage over ordinary cod liver oil as a source of nutriment which is claimed for it by the manufacturers. Street emphasizes that the Wampole preparation does not possess to any marked degree the reconstructive properties of cod liver oil, butter fat and egg yolk, on which foods rats gain weight rapidly and steadily after having been on a deficient diet. Street calls attention to the fact that the amount of alcohol consumed daily by the user

of the Wampole preparation (the equivalent of 0.7 fluid-ounces of whiskey) explains to a considerable extent the asserted tonic virtues of the preparation.

Though offered as an efficient substitute for cod liver oil, Wampole's "Perfected and Tasteless Preparation of an Extract of Cod Liver" lacks both the nutritive and the reconstructive properties and is marketed under an indefinite name and unwarranted and untrue claims. It is recommended that Wampole's Preparation be held ineligible for New and Nonofficial Remedies.

Veracolate

(From The Journal A. M. A., April 24, 1915, p. 1440)

"Veracolate (plain)," "Veracolate with Pancreatin and Pepsin" and "Veracolate with Iron, Quinine and Strychnine" are proprietary tablets marketed by the Marcy Company, Boston.

"Veracolate (plain)."—For this the following non-quantitative formula is given:

"A compound containing the bile acids, sodium glycocholate, sodium taurocholate with cascara sagrada and phenolphthalein."

The dose is three tablets. Examination in the Chemical Laboratory of the American Medical Association of a specimen of "Veracolate (plain)" indicated that there was about 20 mg. (⅓ grain) of phenolphthalein to each tablet. One dose, therefore (three tablets), would contain 1 grain of phenolphthalein—an average dose.

"Veracolate with Pepsin and Pancreatin."—The following "formula" is given for this mixture:

"Veracolate	1¼ grain
"Pure Pancreatin	1 grain
"Pepsin aseptic (1: 3,000)	½ grain
"Oil peppermint	1/10 min."

(Note the presence of two mutually incompatible digestive ferments.)

"Veracolate with Iron, Quinine and Strychnine."—This is stated to have the following "formula":

"Veracolate	1⅛ grain
"Reduced Iron	1 grain
"Quinine Sulphate	⅜ grain
"Strychnine Sulphate	1/100 grain"

It will be noticed that these mixtures increase in complexity until a combination of seven diverse ingredients, a veritable shotgun mixture, is evolved. In none of the "formulas" are the proportions of the purgative drugs in Veracolate stated. In the second "formula," the digestants might

as well be omitted, for the pancreatin is destroyed by peptic digestion and hence cannot pass the stomach while the pepsin is useless without hydrochloric acid, and, at any rate, of no value in the intestine. If one is indicated, the other is not. Yet this unscientific and complex combination of purgatives, mutually incompatible digestive ferments, and oil of peppermint is called:

"A scientific Blending of Digestive Ferments, Cholagogues and Carminatives."

". . . for all forms of indigestion and dyspepsia."

And the third, an equally irrational and complex combination, is termed "The Ideal Cholagogic Tonic"!

Extravagant and Misleading Claims.—True to type, the claims are magnified in accordance with the number of ingredients. For instance, of "Veracolate (plain)," we are told:

"Veracolate is a true cholagogue and biliary disinfectant as it *directly* stimulates the liver cells producing an increased flow of limpid bile. Although not a purgative, it moves the bowels and is definite and dependable in its action."

"The action of Veracolate is to bring about a profuse flow of healthy bile which prevents bile stasis. As the flow of bile is stimulated so antiseptic action ensues, calculi softened and the concretion and mucous eliminated. Mucosal swelling is diminished and the infection which is usually present is antagonized. Relief is in plain evidence. As a result of the treatment the skin, eyes and urine become normal in appearance in a short time, the appetite and digestion improve and soreness in the region of the gall-bladder is entirely relieved."

Similarly, it is said of "Veracolate with Pancreatin and Pepsin" that:

"It causes a natural flow of bile which checks fermentation, prevents the absorption of toxines and causes the food elements to be emulsified and thus rendered easy of assimilation. All this conduces to a natural movement of the bowels. Digestion is at once improved and the epigastric pain, nervous symptoms and headache disappear."

"Veracolate with Iron, Quinine and Strychnine" is said to be indicated in:

"Hepatic Torpor accompanied by Anemia, Chlorosis, Debility, Neurasthenia and Neuroses."

And the physician is asked to believe that it will:

". . . give gratifying results in all *nervous, anemic,* and 'run down' conditions in which the liver function is usually subnormal."

The objections to "Veracolate (plain)" are that it is semi-secret in composition, unscientific in combination and exploited under unwarranted claims. The same criticisms hold with reference to "Veracolate with Pancreatin and Pepsin" and "Veracolate with Iron, Quinine and Strychnine."

These products are discreditable to the medical and pharmaceutical profession alike and their use is against the public good. The Council therefore refused recognition to Veracolate and its preparations.

Taurocol

(From The Journal A. M. A., April 24, 1915, p. 1441)

The Paul Plessner Company, Detroit, places on the market Taurocol Tablets and Taurocol Compound Tablets. The company makes a pretense of giving the formula—minus any quantities—thus:

"Taurocol is a combination of bile salts, extracts of cascara sagrada, phenolphthalein and aromatics."

The "formula" given for Taurocol Compound Tablets is:

"Taurocol (Bile Salts)	Gramme	.1296
Pepsin 1-3000	"	.0324
Pancreatic Ext.	"	.0324
Extract Nux Vomica (⅛ gr.)	"	.0081
Aromatics		Q. S."

A comparison of these two "formulas" with those furnished for Veracolate and Veracolate with Pancreatin and Pepsin (see preceding report) shows that they are nearly the same.

The claims made for the Taurocol preparations are essentially those made for Veracolate preparations, as instance the following, which appears on a physician's sample of Taurocol:

"For Hepatic Insufficiency, Intestinal Putrefaction, Habitual Constipation."

Likewise the following, found on a Taurocol circular, duplicates claims made for Veracolate:

". . . Directly stimulates the liver cells, producing an abundant flow of bile rich in cholates, solvent of cholesterin and a biliary antiseptic."

Taurocol is objectionable for the reasons that apply to Veracolate, and Taurocol Compound Tablets are subject to the objections that apply to Veracolate with Pepsin and Pancreatin. The Council therefore refused recognition to Taurocol and its preparations.

Lactobacilline Omitted from N. N. R.

(From The Journal A. M. A., April 17, 1915, p. 1346)

The Franco-American Ferment Company has advised the Council on Pharmacy and Chemistry that, in advertising its products, it will no longer conform to the rules of the

Council. This is evident. The Franco-American Ferment Company has distributed circulars in which the public is informed that auto-intoxication is the cause of innumerable ills ranging all the way from arteriosclerosis, rheumatism and gout to chronic headache, odorous perspiration, nervous disorders and melancholia; that the Bulgarian bacillus "is a wonderful corrective or remedy" for all these conditions, and that the Lactobacilline products are the only preparations of Bulgarian bacillus "to be had in America which bear his [Professor Metchnikoff's] personal endorsement"—by inference, the only reliable products. In view of the action of the Franco-American Ferment Company, and of the tendency of their advertising to cause the public to exaggerate slight ailments into alarming conditions, the Council has voted that the several Lactobacilline products of this concern be deleted from New and Nonofficial Remedies.

Iodex

(*From The Journal A. M. A., June 19, 1915, p. 2085*)

Iodex is manufactured by Menley and James, Ltd., New York. It is advertised as

". . . an embodiment of vaporized iodin in an organic base, reduced and standardized at 5 per cent. by incorporation with a refined petroleum product."

The advertising conveys the impression that the effects of free iodin are to be obtained from the preparation; it is said to contain "5 per cent. Therapeutically Free Iodine," and to do

". . . everything the doctor expects of FREE iodin employed by inunction, without one physical or therapeutic drawback."

The statements are also made that the preparation "neither stains, irritates, blisters or cracks the skin," and that "thirty minutes after inunction iodin can be found in the urine."

The following report of an examination made by the Chemical Laboratory of the American Medical Association has been submitted to the Council:

"Iodex is dark green, practically black. The green color is apparent when the ointment is rubbed on the skin, but disappears on continued rubbing. This nonstaining property is explained by the results of a test for free iodin, made on five specimens, four of which yielded only minute traces of free iodin, while the fifth yielded none. Of course, the statements that Iodex is an 'Effective Free Iodin Application Without Drawbacks' and also a means of 'Really Efficient External Iodine Therapy Without Stain or Irritation' con-

tradict each other. Free iodin cannot be present in a sufficient quantity to be therapeutically efficient in any application which does not stain or irritate the skin.

"The total iodin content of the five specimens was found to be 2.63 per cent.—a little over one-half of the content claimed.

"Absorption and excretion experiments were performed to test the claim that 'thirty minutes after inunction iodin can be found in the urine.' In several subjects, from 1 to 2 gm. of Iodex was rubbed on the skin of the forearms, and the urine, for periods varying from seven to seventy-two hours, was collected and tested for iodin. In all of the tests the results were negative."

Iodex is advertised as beneficial in muscular soreness, sprains, sciatica, neuritis, chronic rheumatism, enlarged glands, orchitis, epididymitis, gout, burns and dermatomycoses. It is also said to be "Indicated in Glandular Enlargements, Inflammatory Conditions, Various Joint Diseases, Rheumatism, Skin Diseases, Chilblains, etc., etc."

To sum up:

1. As shown in the foregoing laboratory report, the composition is incorrectly stated, for the actual iodin content is only about half of that claimed.

2. It is not true that the action of Iodex is essentially that of free iodin, which is the impression conveyed by the advertising.

3. The assertion made in the advertising, that iodin may be found in the urine shortly after Iodex has been rubbed on the skin, has been experimentally disproved.

In view of these findings, the Council voted that Iodex be refused recognition for conflict with Rules 1, 4 and 6.

Venodine

(From The Journal A. M. A., June 26, 1915, p. 2155)

Venodine (The Intravenous Products Co., Denver), according to information sent to the Council, is "an Intravenous Iodine Compound" put up in ampules each of which contains "28 grains of Sodium Iodide, ⅛ grain each of Beechwood Creosote and Guaiacol in a suitable vehicle, and excipients to enhance its compatibility with the circulating blood."

The "Therapeutic Indications" include "infectious diseases, such as syphilis, tuberculosis, bronchitis, bacteraemias associated with chronic and acute nephritis (Bright's disease), and other infections." The Council held as unwarranted and grossly exaggerated the following therapeutic claims: (1) that the full therapeutic value of iodin medication cannot be readily obtained except by intravenous injection; (2) that

Venodine is "of exceptional value in tuberculosis"; (3) that in pneumonia Venodine "combines the anaesthetic properties of creosote and guaiacol with the germicidal value of iodine"; (4) that "Venodine (or its iodine component) has long enjoyed an exceptional reputation" as of great value in many infectious diseases including bacteremias. The facts on these points are the following:

1. Since iodids are easily absorbed from the mucous membrane of the gastro-intestinal tract and are usually well tolerated by the stomach, there is no reason for resorting to intravenous injection in their administration.

2. The indiscriminate administration of iodids for pulmonary tuberculosis is strongly to be condemned. The cases in which they can be given to tuberculous patients without doing harm must be very carefully selected.

3. There is no evidence either that creosote is excreted by the lungs in sufficient quantity to exert an anesthetic influence or that iodin is present in the circulation of the lungs or in the bronchial secretions in a form which is capable of exerting any germicidal action whatever.

4. It is generally held that the systemic administration of iodin compounds in bacteremias is useless.

The Council also held the name "Venodine" objectionable in that it fails to indicate the chief ingredient (sodium iodid) of this simple pharmaceutical mixture. The statement in a circular that "Venodine is a sterile solution representing 1.54 Gm. (24 grains) of iodine in chemical combination together with creosote and guaiacol" is likely to lead physicians to use the preparation without considering that its chief constituent is the well-known substance sodium iodid, particularly so since no reference to sodium iodid is made in the circular.

Furthermore, the Council held that the combination of two such similar substances as creosote and guaiacol (the second a constituent of the first) as given in the published formula, stamps Venodine as unscientific; it adds mystery to the preparation, but does not increase its efficiency, and is therefore against the best interests of the public.

The Council voted that Venodine be held ineligible for conflict with Rules 6, 8 and 10.

This report having been submitted to the manufacturers, in accordance with the Council's regular procedure, and the reply affording no reason for modifying the findings, its publication has now been authorized.

Calcreose

(From The Journal A. M. A., June 26, 1915, p. 2155)

In response to inquiries and in view of the extensive advertising propaganda, the Council, on Dec. 19, 1913, took up for consideration Calcreose (Maltbie Chemical Company, Newark, N. J.). Examination showed that the preparation contained, in loose combination, approximately equal weights of creosote and lime. The claims made in the advertising "literature" were extravagant and uncritical, and the Council therefore held Calcreose ineligible for New and Nonofficial Remedies.

In June, 1914, at the request of the Maltbie Chemical Company, the Council undertook a reconsideration of the preparation. The advertising claims were now found more conservative. Before the existing claims could be judged, however, the Council deemed it necessary to require from the company satisfactory proof (1) that the large doses of Calcreose recommended and administered actually furnish large amounts of creosote to the blood, and (2) that patients taking these large doses do not suffer from digestive disturbances, loss of nutrition, albumin in the urine or phenol urine, as claimed. The Council accordingly advised the company of this requirement, at the same time stipulating that nothing in the report should be interpreted as indicating a belief on the part of the Council that enormous doses of creosote are necessary for, or will promote a cure of tuberculosis.

The Maltbie Chemical Company has not up to the present date furnished this proof, but has evinced a disposition to make the Council's holding Calcreose under advisement appear in the guise of a quasi-approval. It is therefore recommended that Calcreose be refused recognition for conflict with Rule 6.

Standard Radium Solution for Intravenous Use

(From The Journal A. M. A., June 26, 1915, p. 2156)

Standard Radium Solution for Intravenous Use (Radium Chemical Co., Pittsburgh) is sold in ampules each containing radium bromid equivalent to 0.05 microgram radium element and 0.0002 gm. or less of barium bromid dissolved in 2 c.c. sterile normal physiologic salt solution.

While the Council has confirmed the claimed composition of Standard Radium Solution for Intravenous Use so far as concerns the radium content, it refused recognition to the preparation because there is no clear evidence that intravenous injection has any advantage over the other methods of

administering radium. The Council holds that radium for internal medical use is in an experimental stage, that, on the basis of our present knowledge, this substance should be used intravenously only by those in a position to study its effect carefully, and in an institution equipped with the necessary facilities for such study. For these reasons and on account of the risk involved with any form of intravenous medication, the Council voted not to accept Standard Radium Solution for Intravenous Use for inclusion with New and Nonofficial Remedies.

In accordance with the Council's regular procedure this report was submitted to the Radium Chemical Company for comment. The Council, after considering the new evidence offered, decided that its previous action should be allowed to stand and accordingly authorized publication.

Rheumalgine

(From The Journal A. M. A., June 26, 1915, p. 2156)

Rheumalgine (Eli Lilly & Co., Indianapolis) is put up both in tablet form and as a liquid. Each tablet, or teaspoonful of the liquid, is said to contain:

"Strontium salicylate from Natural Oil..... 5 gr.
Hexamethylenamin ..... 2 gr.
Colchicine ..... 1/200 gr."

The advertising matter contains several statements regarding the individual ingredients to which objection must be made.

It is claimed (quoting from Hare) that strontium salicylate

". . . is not so disagreeable to the taste as the corresponding sodium salts, and more important still, it is far less apt to disorder the stomach."

"Taste" is a difficult subject to dispute; but in the experience of the referee patients object more to the strontium than to the sodium salt. No evidence is submitted to prove that the strontium salt is less apt to disorder the stomach. In observations made under the direction of the referee, the nauseant and emetic doses are about the same as, or even less than, those of sodium salicylate.

Under hexamethylenamin, the recommendations are not confined to its recognized use as a urinary antiseptic; it is also said to be "unexcelled" as a "germicide," and to prevent the formation of urate and phosphate deposits. These statements are contrary to facts.

"Rheumalgine . . . may be used in all cases where the salicylates are indicated. It is superior to preparations containing sodium salicylate, in that it does not cause nausea or disturb the digestion."

Both the preceding statements are misleading. The necessity of giving 1/200 grain of colchicin for each 5 grains of salicylate would certainly interfere with the use of adequate doses of the latter. The colchicin would produce digestive disturbance quite apart from the salicylate.

The mixture is described as:

". . . ANTIRHEUMATIC, ANTIPYRETIC, URINARY ANTISEPTIC, AND URIC ACID ELIMINANT. Useful in Acute Articular and Chronic Rheumatism, Muscular Pains, Lumbago, Sciatica, Migraine of the Rheumatic, Gout, and in Nervous Irritability of the Gouty or Lithemic."

The facts are: Salicylates are useful in some of these conditions, colchicin occasionally in a few, hexamethylenamin in none. The combination is conducive to uncritical prescribing. For instance, salicylates are effective in acute articular rheumatism; hexamethylenamin and colchicin are useless; salicylates are of very little use in chronic rheumatism, sciatica and nervous irritability, while hexamethylenamin and colchicin are useless in these conditions; colchicin is sometimes effective in gout, salicylates perhaps also; hexamethylenamin is not.

Attention should also be called to the high dosage of colchicin, namely, 1/100 to 1/50 of a grain of the alkaloid, every three or four hours, the dose then to be "slightly reduced," but continued for several days; or in chronic cases, 1/100 to 1/30 grain per day, continued indefinitely. This dosage appears high, if a really active preparation is used.

Finally, the name "Rheumalgine" encourages thoughtless and unscientific prescribing. If a mixture is used at all, the prescriber should be constantly reminded of its composition.

It is therefore recommended that Rheumalgine be held in conflict with Rules 6 (unwarranted therapeutic claims), 8 (non-descriptive name) and 10 (unscientific composition).

Uricsol

(From The Journal A. M. A., Aug. 14, 1915, p. 638)

Uricsol is marketed by the Uricsol Chemical Company, formerly of Los Angeles, now of Boston. Regarding its composition only vague statements are made. In an advertising pamphlet it is promised that the formula will be sent to physicians on request. Such a request from a physician elicited the following statement:

"URICSOL is a non-irritating, alkaline solution, containing Lithium Citrate, Acid Citric and Potassium Nitrate, together with a saline laxative in the form of Glycero Sodium Phosphate, with Vegetable Tonics added."

The Association Laboratory has made an examination of Uricsol to determine its composition and reports as follows:

LABORATORY REPORT

A trade package purchased in March, 1915, from a wholesale drug house was labeled:

"Uricsol Rheumatic Remedy, Uric Acid Solvent, Kidney and Liver Stimulant, Manufactured by the Uricsol Chemical Co., Los Angeles, Cal."

This package was wrapped in a circular entitled "The Great California Remedy—Uricsol." The preparation is a viscid, slightly turbid light brown liquid, with a faintly aromatic odor and a salty, bitter taste. The diluted solution is acid in reaction toward litmus and phenolphthalein and alkaline toward methyl orange.

Qualitative tests showed a presence of phosphate, citrate, nitrate, sodium, glycerin, and a small amount of lithium in aqueous solution. Besides these a small amount of some organic, nonalkaloidal substance was found, which from its bitter taste suggested gentian. From the qualitative tests it appeared that the phosphate was the predominating ingredient and according a phosphate determination was made. The results, calculated to sodium phosphate, U. S. P., indicated the presence of 64.20 gm. per 100 c.c., held in solution by citric acid and sodium nitrate.

Uricsol evidently is a solution containing a large amount of sodium phosphate with small amounts of lithium, nitrate, citric acid and glycerin with probably some vegetable extract.

In general Uricsol is similar to the once widely exploited proprietary "Melachol," which has been frequently imitated. A preparation essentially identical is in the United States Pharmacopeia, under the title "Compound Solution of Sodium Phosphate."

The Uricsol Chemical Company calls its preparation

". . . the latest word in the treatment of Rheumatism and that allied group of ailments which is caused by an excess of Uric Acid."

Hay fever, bronchial asthma and neuritis are conditions in which it is recommended. The claim is made that

"Uricsol quickly controls Vasomotor Rhinitis and eliminates such conditions from the system." "In fact, it will correct FAULTY METABOLISM."

To a few practitioners of an older generation the pharmacologic basis of a remedy for rheumatism was sufficiently defined by saying that it increased the solubility of uric acid or affected it in some way. This theory is obsolete; there is not, and never was, any reliable evidence on which to base the theory that rheumatism is in any way caused by uric acid. The exploitation of Uricsol as a "uric acid

solvent" is merely another illustration of the way in which nostrum manufacturers play on disproved theories. Of course the claim that sodium phosphate has any particular power to control vasomotor rhinitis, hay fever, asthma, and to correct faulty metabolism is foolish.

To summarize: Uricsol is a mixture of well-known drugs marketed with false claims as to therapeutic action, with misleading and meaningless statements as to composition and under a name which invites uncritical prescribing. Uricsol is held ineligible to inclusion in New and Non-official Remedies.

Duodenin, Armour

(From The Journal A. M. A., Aug. 14, 1915, p. 639)

Duodenin, Armour (Armour & Co., Chicago), supplied in 1 grain and 2 grain tablets, is said to be prepared from the glandular or epithelial layer and mucous lining of the hog duodenum and to contain the maximum amount of secretin and enterokinase in stable form. Armour & Co. claim that the secretin in Duodenin has not been submitted to boiling or precipitation processes or otherwise exposed to possible changes by hydrolysis, and that the administration of the combination of secretin and enterokinase found in Duodenin, Armour, increases the flow of pancreatic juices and at the same time activates the proteolytic enzyme to a maximum. This claim is based on the hypothesis that gastric digestion does not destroy the secretin and enterokinase said to be present in the preparation. The following recommendations for use are made:

"Duodenin (Armour) is recommended in the treatment of intestinal disorders where an increased flow of pancreatic, hepatic and intestinal secretion is desired. It is of specific value in proteid digestion on the theory that secretin and enterokinase stimulate the pancreas and activate its secretion."

Discussing the claims the referee of the Committee on Pharmacology reported to the Council that apparently no investigations have ever shown the existence of conditions in which there is an absence or an insufficient amount of enterokinase and that the existence of such conditions is improbable. He reported further that all adequately controlled physiologic experiments so far reported show (Starling, Matsuo) that pancreatic secretin given by mouth or directly into the intestine, is not absorbed in active form, and that no evidence is available to show that conditions exist in which there is a deficiency of secretin or enterokinase. He held that Duodenin, Armour, should not be considered further until evidence has been submitted to show that there are conditions in which secretin or enterokinase is absent and that these substances may be utilized by the

organism if administered. As all that is known concerning these hormones tends to discredit the assumption that their administration is of use, he recommended that in the absence of any scientific evidence of its therapeutic value, Duodenin, Armour, be not admitted to New and Nonofficial Remedies.

The Council adopted the report of the referee.

Jubol

(From The Journal A. M. A., Aug. 14, 1915, p. 639)

The following ridiculous statements are addressed, not to the laity, but to the medical profession:

"DO YOU SUFFER FROM Constipation—Hemorrhoids—Enteritis—Mucous discharge — Pituita — Acidity of the stomach—Vertigo — Sick Headache — Disturbed Sleep — Insomnia —Sallow Complexion— Coated Tongue— Offensive breath— Fatigue and depression — Boils — Pimples?

"ONE of these symptoms alone shows that there is defective or insufficient function of the intestines, even if the stools are regular.

"Excrements remain too long in the intestine and set up fermentation. The harmful poisons and ptomains which they produce are re-absorbed by the blood and poison the whole system.

"The Intestines must be cleared and re-educated with JUBOL.

"Jubolise your Intestines."

Jubol tablets are sold in the United States by Geo. J. Wallau, Inc., New York, and are said to be prepared by J. L. Chatelain, Paris, France. The following incomplete and non-quantitative "formula" is furnished:

" . . . compounded chiefly [!] of Agar-Agar, Biliary Extracts and pure Extracts from all the intestinal Glands."

It is asserted that

"The tablets are coated with a protective covering in order that they may act on the intestine only."

The tablets contained in a regular-size trade package, obtained direct from the agent, readily separated into two halves and disintegrated within a few minutes when agitated with water. It is thus evident that, under ordinary conditions, the intestinal ferments in Jubol (if they are present, as claimed) would be destroyed during their passage through the stomach. In direct tests, however, practically no tryptic activity was demonstrated.

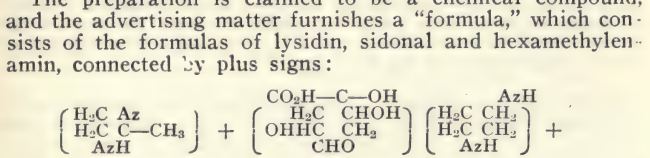
The composition of Jubol is not declared; grossly unwarranted and incorrect claims are made for its therapeutic actions; the name does not indicate the alleged ingredients and so much of the composition as is declared indicates an unscientific mixture. The Council decided that Jubol should be held ineligible for New and Nonofficial Remedies, and that this report should be published.

Urodonal

(From The Journal A. M. A., Aug. 14, 1915, p. 639)

Urodonal is said to be "produced in the laboratory of J. L. Chatelain," Paris, France. It is marketed in this country by Geo. J. Wallau, Inc., New York.

The preparation is claimed to be a chemical compound, and the advertising matter furnishes a "formula," which consists of the formulas of lysidin, sidonal and hexamethylenamin, connected by plus signs:



That the substance is a chemical compound is highly improbable, and no evidence has been submitted to substantiate the claim. On the contrary, in the following statement the phrase "based on" is a virtual admission that the preparation is merely a mixture:

"Urodonal . . . is a granular effervescent preparation based on methylglyoxalidine [Lysidine], quinate of diethylene-diamine [Sidonal] and hexamethylene-tetramine [Formin, urotropine]."

Mystery is added by the mention of undefined "special products" in the following:

"The fact of combining these two salts [lysidin and sidonal] in Urodonal, in strictly determined proportions and in the presence of special products, gives this preparation very considerable power in dissolving uric acid."

These contradictory statements of composition conflict with Rule 1.

Urodonal is marketed in typical "patent medicine" style: the name "Urodonal" is blown in the bottle and the label contains a list of "Indications," including rheumatism, gout and gravel (Rule 4). That this form of marketing has introduced it to the public is suggested by the following in an advertising circular:

" . . . Urodonal is now popular—even classic—throughout the world, where thousands of doctors and millions of patients agree in asserting that 'Urodonal is to rheumatism what quinine is to fever.'"

There are also other indications that the mixture is to be exploited to the laity. For instance, the U. S. distributor sends out a portrait of Sarah Bernhardt bearing the legend:

"I am positive that URODONAL preserves youth's freshness with clearness and strength to brain and heart. I have taken it for two years with the greatest benefit. Sarah Bernhardt."

A circular advises this mixture

"For all who suffer from Arthritis, Rheumatism, Arterio-Sclerosis, Renal and Bilious Lithiasis, Headache, Gout, Gravel, Lumbago, Sciatic Pains, Neuralgia and all uric acid troubles."

"In fact, Urodonal is five times more active than piperazine, and thirty-seven times more active than lithia. We are, therefore, entitled to say that no other eliminator of uric acid can be compared with it."

"Being *37 times more active than lithia,* it clears the heart valves of any sandy substances which may clog them, and checks the atheromatous degeneration of the blood vessels."

These extracts indicate sufficiently the extravagant tone of the advertising (Rule 6): None of the ingredients are notably active in dissolving uric acid when administered by mouth. None produce any marked increase of uric acid elimination. No intelligent physician would use a uric acid solvent for "bilious lithiasis"; and their usefulness in the other conditions is open to doubt, to put it mildly.

Although the preparation is a simple mixture, the name does not indicate the components, but inclines to therapeutic suggestion (Rule 8).

Nothing is to be gained by combining several drugs which are useless, severally, for the purpose intended, as in the present case (Rule 10).

Urodonal is marketed under inconsistent statements of composition and with exaggerated therapeutic claims; the name is nondescriptive and the mixture is unscientific. The Council decided that the preparation should be declared ineligible for conflict with Rules 1, 4, 6, 8 and 10 and that this report should be published.

Hydragogin

(From The Journal A. M. A., Sept. 4, 1915, p. 894)

Hydragogin (C. Bischoff & Co., New York, selling agents) is advertised as "a most powerful diuretic and cardiac tonic." The composition given is:

"Fifteen parts of the remedy contain 0.5 parts oxysaponin, 1.5 parts tincture of digitalis, 2.5 parts tincture of strophanthus, scillipicrin and scillitoxin, the active principles of scilla maritima, and alcohol."

It is not clear from this statement whether 15 parts of Hydragogin contain 2.5 parts of tincture of strophanthus, plus unspecified amounts of scillipicrin and scillitoxin, or 2.5 parts of a mixture, in unspecified proportions, of tincture of strophanthus, scillipicrin and scillitoxin. The activity of strophanthus, after it enters the blood stream, is about fifty times that of digitalis; hence, if the former proportion is the true one, in giving an amount of Hydragogin which ensures the full therapeutic effect of the digitalis, one would administer an almost certainly fatal amount of strophanthus. Whatever the proportion of strophanthus may be, however, the

administration of a mixture of digitalis and strophanthus in fixed proportions is indefensible. At times it is advisable to follow one of these drugs with the other in the treatment of cardiac disease. The simultaneous administration of the two continuously in fixed proportions, however, is injudicious, because of the great difference between their rates of absorption and in their activity after they enter the blood stream. The action of digitalis, moreover, persists much longer than does that of strophanthus.

An advertising circular contains the following claim:

"The well-known diuretic properties of digitalis, strophanthus and squills are greatly enhanced by the addition of the oxysaponin."

This is not true. Saponins are not synergistic with digitalis therapeutically; on the contrary, they exert a purely deleterious action on the heart when they enter the circulation.

The symptoms of cardiac disease are often difficult to distinguish from the toxic actions of the digitalis bodies. Since these bodies must often be given to the point of beginning toxic action in order to induce the full therapeutic effects, it is obvious that the administration of a mixture of digitalis, strophanthus, saponin and active principles of squill is especially liable to induce serious toxic effects which cannot be distinguished from the symptoms of the disease.

Hydragogin is a shotgun mixture of semisecret composition; it is marketed under a therapeutically suggestive name, and advertised by means of unwarranted therapeutic claims. It is therefore in conflict with Rules 1, 6, 8, and 10. The Council held Hydragogin ineligible for New and Nonofficial Remedies.

Williams' Syrup of Malt

(From The Journal A. M. A., Sept. 4, 1915, p. 895)

Williams' Syrup of Malt (The American Malt Extract Co., San Francisco) is essentially a simple malt extract. It is evident, therefore, that the following claim, which appears on the trade package, is without warrant:

"As a tonic and tissue builder it is invaluable. Especially beneficial in cases of diabetes, consumption, kidney, liver and stomach troubles."

Also, the following claims, which appear in a circular:

"Williams' Syrup of Malt is a powerful agency for *Building Tissue.*"

"When indicated with Nursing Mothers it stimulates the Mammary Glands and not only increases the quantity of milk, but enriches the quality."

"We also emphasize its beneficial qualities in the incipient stages of tubercular diseases and for stomach disorders and Diabetic conditions."

The Council held Williams' Syrup of Malt ineligible for N. N. R. because it is essentially an official preparation sold

under an unofficial title (see N. N. R., 1915, p. 14); because unwarranted therapeutic claims are made for it and because the claims made are apt to lead the public to depend on it as a curative agent in serious diseases.

Filudine

(From The Journal A. M. A., Sept. 18, 1915, p. 1045)

Filudine is said to be prepared by J. L. Chatelain, Paris, and is sold in this country by Geo. J. Wallau, Inc., New York. It is offered as a remedy for "biliary insufficiency," "hepatic insufficiency," "intestinal dyspepsia," "all affections of the liver (diabetes, cirrhosis, cancer, etc.)," "malaria," "obesity" and "tuberculosis."

No quantitative information is furnished as to the composition of the preparation and there are noteworthy discrepancies in the various statements regarding the ingredients. In one number of "Treatment," a self-styled "Review" of medical literature (actually devoted to advertising the preparations sold by Wallau), we are told that

"This product [Filudine] is a more concentrated and potent extract of the liver, with which is combined an extract of the spleen. The liver and the spleen are so intimately interdependent, that the addition of a splenary extract to the liver extract is a signal improvement from which a synergistic action results. Thiarféine is also added, as it helps somewhat to combat the anaemia from which all diabetics suffer more or less."

Thiarféine is said to be

"Thiomethylarsinate of Caffein, a new salt discovered by M. Chatelain."

Another circular, which gives an imposing formula for "thiarféine" or "thiomethylarsinate of caffein," states that

"Sulphurated methylarsinate is an arsenical preparation devoid of all toxicity on account of the intimate joining of its composing parts."

And that

"Filudine can never be contraindicated . . ."

A statement of composition in a later number of "Treatment," however, says that biliary extracts are components, in addition to the liver and spleen extracts. Moreover, thiarféine, the "new salt discovered by M. Chatelain," is no longer "thio-methyl arsinate," but "thio-cinnamate of caffein"; and a new formula is furnished for it.

We are told that

"Methyl-arsinate cannot be used in cases where fever is present. . ."
"M. Chatelain at first studied the action of thiomethylarsinate; clinical and physiological experimentation led him, however, to adopt thio-cinnamate of caffeine, of greater activity and with no contraindications."

Nevertheless the same absence of contraindications was urged in favor of Filudine when it was said to contain the now discarded thio-methylarsinate of caffein.

The following are some of the unwarranted and even absurd claims:

"Filudine restores the liver's functions. It is to the liver what digitalis is to the heart; it overcomes the insufficiency and stimulates the debilitated organ."
In malaria "it is the only true specific when associated with quinine."
"Filudine is . . . the ideal medication for tuberculosis, conforming as it does with the most recent researches in the therapeusis of this affection."
"We will not go as far as to say that Opotherapy *completely restores* unhealthy livers, for although the lesions of the hepatic parenchyma may be obliterated by regeneration, the lesions of the connective tissues are permanent, and may be observed at the postmortem examination. The new cells however do not present the same unhealthy conditions as those of the former diseased gland which they have replaced, and the liver can therefore function normally, so that the patient lives on; and he is satisfied with that."
"Therefore, while regenerating the liver with Filudine, we cleanse it and combat its congested state with Urodonal. We cause it to produce urea from the excess of uric acid which it contains."
"By the judicious and harmonious combination of the beneficial effects of Filudine and Urodonal, physicians not only possess the means of treating by rational methods Cirrhosis of the Liver in its various forms (which is one of the most terrible diseases which can afflict anyone) but what is still better, *they can cure it.*"
"The liver of a person suffering from obesity being incapable of fulfilling its functions in regard to the fatty tissues, the rational and up-to-date method of treatment is therefore to restore to the system, in the form of Filudine, the liver extracts which are lacking."

Filudine is a mixture of semisecret composition. The therapeutic claims are manifestly unwarranted. The name is not indicative of the composition, whatever that may be, and no rational excuse is offered for the combination of liver and spleen extracts (with or without bile extracts) with "thio-methyl arsinate" or "thio-cinnamate" of caffein.

The Council therefore held Filudine ineligible for New and Nonofficial Remedies.

Globeol

(From The Journal A. M. A., Sept. 18, 1915, p. 1046)

Globeol is prepared by J. L. Chatelain, Paris, and sold in this country by Geo. J. Wallau, Inc., New York. It is advertised in a pamphlet also exploiting Urodonal, Jubol and Filudine. It is open to the same objections as these prepara-

tions—incomplete statement of composition, pseudoscientific statements of its actions and absurdly exaggerated statements of its value.

Globeol is thus described in a pamphlet:

"Globeol is the total extract of the red globules with the exception of its outer portion, and is obtained by powerful centrifugalization of the blood mixed with 20 parts of isotonic liquid, and subjected to several successive refrigerations in vacuum. . . .

"The blood used is obtained from young and healthy horses, after they fasted and rested on the previous day. The serum is put aside and desiccated in vacuum at a low temperature. The dry serum obtained in the shape of an amber yellow powder, is mixed with Globeol. In it are to be found in their full activity such bodies as precipitins, agglutinins and antitoxin, as well as internal secretions of organs arousing certain glandular synergies.

"Moreover, the action of Globeol has been strengthened by the presence of colloidal iron and colloidal manganese (which supply the deficiency in mineral salts) and also by the addition of a very small quantity of quassia as a means of preparing the digestive organs for the absorption of more food."

When the description is divested of obscuring verbiage, Globeol appears to be evaporated horse blood, mixed with small quantities of colloid (dialyzed?) iron and manganese, and a dash of quassia. No information is given as to the quantities of these ingredients.

A mixture of this kind should act like a simple hematinic. Since every physician knows the value and limitations of the hematinics, and has a wide choice of standard and efficient articles, there is no necessity of employing a complex substance of unknown composition unless it has some real advantage. Accordingly, the superstitious awe of the blood as a most particular juice is invoked, and this is apparently illuminated by such terms as "protoplasmic pulp"; "blood ferments in their active state (oxydases, catalases, stimulins, etc.)": "precipitins, agglutinins and antitoxin, as well as internal secretions of organs arousing certain glandular synergies"; "living ferments"; "energising substances of cellular activity"; "phagocytic microbes"; "vitalized" iron manganese; "positive chemotaxis"—in brief, "opotherapy of the blood by means of its active ferments"; but the exploiters forget to mention that these various "ins" and ferments, as well as the hemoglobin and proteins, are broken down in the digestive tract and never reach the blood. Most fortunately; for if they did so, the Globeol would certainly play havoc with the patient.

It is difficult to preserve patience when such dense ignorance is shown in the "literature" that presumes to instruct the profession.

The therapeutic claims and testimonials may be dismissed by citing a few illustrations, plainly in conflict with Rule 6:

"These ingredients, when introduced in the blood, impart to it renewed strength, and augment the patient's vitality. He feels as if he were resuscitating."

"Microbes secrete poisons which are very dangerous, and the human organism endeavors to combat these poisons by natural means. The faculty is however very much impaired in the case of debilitated, run-down or over-worked persons. Globeol, by introducing anti-toxins into the blood, combats the noxious microbes of affinity called "Positive Chemotaxis," besides stirring up the protective faculties of the tissues by favouring the formation of their own anti-noxious elements. This action is further increased by the presence of colloid minerals, which, as is perfectly well known, are endowed with a well determined anti-toxic faculty."

"It is a remedy for anemia and chlorosis, and a sovereign cure in all cases of organic decomposition arising from any cause whatsoever, whether it be overwork, too rapid growth, convalescence, scrofula, tuberculosis, ataxia, cancer, diabetes, cerebral anemia (anemia of the brain), malaria, general and nervous debility, etc."

"The invasion of the system by the tuberculous poison, that is, by the toxins which the bacillus of Koch produces, is overcome by means of the anti-toxic ferments in the red corpuscles which are contained in globeol in a state of activity, and which render inert the toxic action of the microbes."

"Physicians who have tested the value of Globeol, agree in saying that all healthy individuals should take a course of Globeol in spring and autumn as a preventive, in order to stimulate the production of blood, strengthen the system, and by invigorating it, enable it to resist the attacks of disease."

"Neurasthenia cannot resist Globeol, and I have seen numerous cases of rapid and permanent cure."

The Council declared Globeol ineligible to N. N. R. because it conflicts with Rules 1, 6, 8 and 10.

Hexa-Co-Sal-In

(*From The Journal A. M. A., Oct. 2, 1915, p. 1203*)

Hexa-co-sal-in (Hexa-Co-Sal-In Company, Red Bank, N. J.) is advertised as "a condensation product of familiar composition." The further explanation that it is "colchi-magnesium salicylate with anhydrous hexamethylenamin" does not make this statement much clearer. "Colchi-magnesium salicylate"—not to speak of its condensation product with hexamethylenamin—is unknown in chemical literature. As a matter of fact, an examination made by the Chemical Laboratory of the American Medical Association shows that Hexa-co-sal-in is a simple mechanical mixture of hexamethylenamin, magnesium salicylate and some colchicum preparation. The composition is therefore falsely stated.

The preparation is advertised as:

"Antirheumatic, Antineuritic, Urinary Antiseptic."
"Uric Acid Mobolizer" (sic).
"Intestinal Antiseptic, Mildly Laxative."
"Whenever a salicylate is indicated use Hexa-co-sal-in."

The combination of salicylates, hexamethylenamin and colchicum in a routine formula is certainly inadvisable; where one of the ingredients is needed, the others may be useless or even harmful. The unqualified advice to use hexamethylenamin and colchicum "whenever a salicylate is indicated" is likely to do harm.

The statement of the composition of this preparation is false; unwarranted therapeutic claims are made for it, and the mixture is unscientific. The Council held Hexa-cosal-in ineligible for New and Nonofficial Remedies because of conflict with Rules 1, 6 and 10.

Swan's Rheumatic Bacterin (Mixed) No. 47

(From The Journal A. M. A., Nov. 6, 1915, p. 1662)

According to the statement of the manufacturers (Swan-Myers Company, Indianapolis, Ind.), Swan's Rheumatic Bacterin (Mixed) No. 47 contains in each c.c., pneumococci 25,000,000, Friedländer's bacilli 25,000,000 and streptococci polyvalent 450,000,000.

The Council's Committee on Serums and Vaccines held that there is no satisfactory evidence that either the pneumococcus or Friedländer's bacillus is concerned in the etiology of acute and chronic rheumatism or rheumatoid arthritis, and no conclusive evidence that the streptococcus is an etiologic factor. In view of this the committee held this mixed vaccine unscientific in composition, and hence barred from admission to New and Nonofficial Remedies by Rule 10.

The Council adopted the report of the committee and, the report having been sent to the manufacturer in accordance with its regular procedure, and the manufacturer's reply considered, authorized its publication.

Elixir Iodo-Bromide of Calcium Comp. "Without Mercury" and "With Mercury"

(From The Journal A. M. A., Nov. 6, 1915, p. 1662)

The Tilden Company, New Lebanon, N. Y., and St. Louis, Mo., sells "Elixir Iodo-Bromide of Calcium Comp. without Mercury" and "Elixir Iodo-Bromide of Calcium Comp. with Mercury." The latter is said to contain, in addition to the ingredients of the former, $\frac{1}{100}$ grain mercuric chlorid in each fluidram. According to the label the formula of the elixir "without mercury" is :

"*Formula*—Salts of Iodine, Bromine, Potassium, Sodium, Calcium, Magnesium with Stillingia, Sarsaparilla, Rumex, Dulcamara, Lappa, Taraxacum, Menispermum."

A recent circular declares that the elixir contains:

". . . a number of the most powerful alteratives of the pharmacopeia such as chemically pure iodin, magnesium, potassium with sarsaparilla, stillingia, prickly ash, burdock, taraxacum, etc. . . . Each fluidounce contains seventy-two grains of the combined salts."

The same circular also alleges that each dram of the preparation contains:

". . . the equivalent of one and one-half grains of the combined iodids, potassium and calcium . . . "

It will be observed that, (1) the two statements quoted from the circular make no reference to bromids; (2) the statement that each dram contains "the equivalent" of 1½ grains of the combined iodids, potassium and calcium, accounts for but 12 of the 72 grains of "the combined salts" per fluidounce declared in the preceding quotation; (3) the circular mentions the presence of a drug—prickly ash—not declared on the label and, finally (4) none of the "formulas" gives the quantities of all of the several constituents.

It is evident from these "formulas" that the Tilden Company continues its policy of concealment and mystification as exemplified in the cases of Hydrocyanate of Iron, Tilden (discussed in THE JOURNAL, June 19, 1909, p. 2008), Febrisol (THE JOURNAL, June 29, 1912, p. 2043) and Respirazone (THE JOURNAL, June 14, 1913, p. 1899).

In the circular just quoted ("The Conquest of Syphilis"), all hope for the syphilitic is declared to rest in mercury and iodin, and it is implied that only through Elixir Iodo-Bromide of Calcium Comp. is it possible to obtain the greatest good from these drugs.

"Were the cleansing influences of these two drugs [mercury and iodin] unavailable to the luetic patient, he, truly, would be as pitiable an object as the leper . . .

"Modern Pharmacy has devised no better means of utilizing these anti-syphilitics than Elixir Iodo-Bromide of Calcium Comp. (Tilden) with or without mercury. . . . the Elixir, in proper dosage, acts in specific fashion and is adapted for use in all stages of the disease.

"In the early months . . . Elixir Iodo-Bromide of Calcium Comp. (Tilden) with mercury is a trustworthy weapon and the physician need have no fear but that it will subjugate the disease . . .

"When . . . the virulent stage is passed . . . Elixir Iodo-Bromide of Calcium Comp. (Tilden) without mercury may be given the patient with every assurance that medicine's most aggressive measures are being resorted to . . . From time to time, up to the very end of the time honored three years' period of treatment, it is well to put the patient back on the bichloride, using for this purpose the form of the Elixir administered in the first stages of the disease . . .

"This regime . . . will indubitably antidote the virus of syphilis and eradicate from the organism its every vestige."

While it seems incredible that any physician would jeopardize the health—even the life—of a patient by accepting this boastful magniloquence as sound therapeutic advice, still the fact that certain medical journals lend their advertising pages to advertisements for Tilden's Elixir with the caption "The Conquest of Syphilis" makes it incumbent on the Council to record its condemnation of the employment of this unscientific, semisecret mixture.

It is recommended that Elixir Iodo-Bromide of Calcium Comp. "without mercury" and "with mercury" be held in conflict with Rule 1 (secrecy of composition), Rule 6 (unwarranted therapeutic claims) and Rule 10 (unscientific composition).

Agurin Tablets, Alypin Tablets, 3⅓, 1⅛ and ¾ grain, Hedonal Tablets 8 grains, Iodothyrine Tablets, 5 grains, Tannigen Tablets, Cocaine and Adrenalin Ointment-M. E. S. Co., Dolomol Pyrogallic Acid 5 per cent., Dolomol Chrysarobin 5 per cent., Dolomol Europhen 10 per cent., Dolomol Naphthol 5 per cent., Dolomol Salol 10 per cent., Dolomol Tar 10 per cent., Dolomol Thymol 2 per cent. and Xerase Capsules Omitted from N. N. R.

The Council was informed by the owners or American agents of the above-mentioned dolomol products (Pulvola Chemical Company, New York), of the above-mentioned agurin, alypin, hedonal, iodothyrine and tannigen tablets (Bayer Company, New York), of cocaine and adrenalin ointment-M. E. S. Co. (Manhattan Eye Salve Company, New York) and of xerase capsules (Riedel and Co., New York) that the sale of these dosage forms has been discontinued. (The dosage form of xerase — xerase capsules — was withdrawn from the market, the manufacturers reported, because the capsules were found not to dissolve readily.) Accordingly the Council voted to omit mention of these dosage forms in future editions of New and Nonofficial Remedies.

Anistamina

Anistamina (U. S. agent M. Olivetti) is a tuberculosis remedy said to be prepared by Dr. Carlo Marchesini, Genoa, Italy. The following formula is furnished in the letter of submission:

Formolacto-guaiacolo ..... gr. 1.685
(Ac. form. gr. 37-38—latt. 37-1 guaiac. 25.22)
Fosfoemoglobina ..... gr. 0.661
(Emogl. gr. 95.30—ac. fosf. 4.70)
Iodotanno-guaiacolo ..... gr. 1.406
(Iodo. gr. 2.21—tann. 67.57—guaiac. 30.32)
Mentolo crist. ..... gr. 0.031
Alc. etil.—glic. bic.—Acq. dist. q. s. p. gr. 100

Making allowance for evident errors, apparently the claim is that the preparation contains guaiacol formolactate, phosphohemoglobin, guaiacol iodotannate and menthol in a water-glycerin-alcohol menstruum.

A circular in several languages, however, declares it to be

". . . a crystalline extract of pulmonary parenchyma. . . ."
". . . une preparation opothérapeutique 'extractum crystallinum et solutum e parenchimate pneumonico medicato' . . ."

No explanation is offered for the discrepancy between the statement of composition furnished in the advertising circular and that submitted to the Council by the American agent; nor is any evidence furnished regarding the existence and identity of guaiacol formolactate, phosphohemoglobin and guaiacol iodotannate.

Neither statement of composition is clear enough to permit of discussion.

Among the therapeutic claims made for the preparation are the following:

"Anistamina acts upon pulmonary tuberculosis, the Peritoneum, the Intestines and osseous tissue."
"1st. It kills the bacillus of Tubercle.
2nd. It neutralises the toxins created by the bacillus of tubercle.
3rd. It induces the cicatrization and healing of the affected lung."

The further statement is made, without condition, that

"In a general way, the cure may be said to take from two to six months."

If all these claims were true, there could be no possible excuse for the continued existence of tuberculosis.

The circular further states that increased cough, hemoptysis and diarrhea are not to be regarded with anxiety or as an indication to stop the treatment. The diarrhea

". . . may be explained by the fact that the stomach and intestines are likewise getting rid of the mucus which covers the lining membrane of these organs."

These statements are as vicious as any in the advertising of the worst "patent medicine" consumption fakes.

The composition of Anistamina is secret and the therapeutic recommendations made for it are not justified by any evidence submitted. The Council refused recognition to Anistamina because of its conflict with Rules 1 and 6.

In accordance with the Council's procedure the preceding report was sent to M. Olivetti for consideration. In reply M. Olivetti wrote that, in view of the Council's findings, he would refuse to handle the preparation. As a matter of record the Council directed publication of this report.

Antipyrin Salicylate-Farbwerke, Betanaphthol Benzoate-Heyden, Betol-Heyden, Bornyval, Euphorin, Eupyrine, Fortoin, Quinine Lygosinate, Sodium Lygosinate, Friedlaender Bacterin-Mulford, Predigested Liquid Food-Mulford, Guaiacodeine and Gujasanol Omitted from N. N. R.

The Council was informed by the Farbwerke Hoechst Company, American agent for antipyrin salicylate-Farbwerke, and by the Heyden Chemical Works, New York, American agent for betanaphthol benzoate-Heyden and betol-Heyden, that these brands are no longer offered for sale in the United States. Accordingly the Council voted that these brands of the respective products be omitted from future editions of New and Nonofficial Remedies. The Council passed a similar vote in the cases of bornyval (Riedel and Co., New York) guaiacodeine (New York Quinine and Chemical Works, New York) and euphorin (Fabrik von Heyden, Radebeul, Germany), on being informed by the owners or American agents that these products also are not offered for sale in the United States; also in the cases of eupyrine, fortoin, quinine lygosinate and sodium lygosinate (C. Bischoff and Co., New York), of Friedlaender Bacterin-Mulford and predigested liquid food-Mulford (H. K. Mulford Company, Philadelphia) and of gujasanol (Farbwerke Hoechst Company), which, according to information furnished by the respective owners or agents, have been withdrawn from the market.

Frosst's Blaud Capsules

Frosst's Blaud Capsules and Frosst's Blaud, Arsenic and Strychnine Capsules were submitted to the Council by C. E. Frosst & Co., Montreal, Canada. This firm claims, on the authority of the report of a firm of analytical chemists, that:

". . . of three leading Blaud preparations bought by us on the open market, the iron in Frosst's Blaud Capsules showed the highest percentage of *Ferrous* carbonate."

The Chemical Laboratory of the American Medical Association found this claim unjustified. The laboratory reported that there was no especial difference in the ferrous iron content of the various Blaud pills found on the market, and that among ten specimens examined, the total iron content was the lowest in the Frosst specimen. In view of this the Council refused recognition to Frosst's Blaud Capsules and Frosst's Blaud, Arsenic and Strychnine Capsules.

Brobor (Episan)

Episan tablets, an epilepsy treatment manufactured by Fa. Episan Berensdorf, Berlin, and sold in the United States by

the Gaynor-Bagstad Co., Sioux City, Iowa, were found ineligible for New and Nonofficial Remedies because the quantitative composition of the tablets was not furnished; because the preparation was advertised indirectly to the public; because the name of the pharmaceutical mixture did not indicate the potent constituents and because the use of a complex mixture of indefinite composition is contrary to the best interests of scientific medicine and the public. The findings of the Council were sent to the American agent for consideration.

In due time the agent submitted a reply from the manufacturer. 1. The composition of the tablets was stated to be potassium bromid 44.30 per cent., borax 41.20 per cent., zinc oxid 3.68 per cent., amyl valerate 4.00 per cent., oil of peppermint 1.00 per cent., coloring matter (amidoazotoluol) 1.82 per cent. and talc 4.00 per cent. 2. It was stated that the indirect advertisement to the public was to be discontinued. 3. It was proposed to replace the name "Episan" by "Brobor." 4. It was argued that the several constituents were of therapeutic value in the treatment of epilepsy and that the combination was rational.

The Council considered the evidence submitted and, on the recommendation of the referee of the committee on therapeutics, voted that Brobor, previously known as Episan, be held in conflict with rules of the Council and therefore ineligible for New and Nonofficial Remedies for the following reasons: 1. The name does not denote the active ingredients that it contains. A physician prescribing the preparation under the name of Brobor would not realize that he was administering borax and therefore would not take the precaution to watch the intestines and the kidneys. Also, he would not realize that the treatment was essentially a bromid treatment. 2. It is a dangerous preparation and has no practical therapeutic value in the treatment of epilepsy except that due to its potassium bromid content. 3. There is no evidence to show that borax is harmless, as claimed, or that either borax or zinc oxid is a nerve sedative.

Bromo-Mangan Omitted from N. N. R.

Bromo-Mangan (made by the Chemische Fabrik Helfenberg A. G., near Dresden, Germany, and sold in the United States by the Reinschild Chemical Company, New York), is a solution said to contain iron, manganese and bromin in combination with peptone. It is sold as a reconstructive tonic, blood-making adjuvant and sedative. It was admitted to New and Nonofficial Remedies in 1907, before the Council had adopted the present Rule 10, which provides that no article shall be admitted to New and Nonofficial Remedies which, because of its unscientific composition, is useless or inimical to the best interests of the public or of the medical profession.

The reason for the use of bromin, manganese and iron in fixed proportions has not been established. The advertising circulars now being used for Bromo-Mangan contain numerous exaggerations. Thus it is stated:

"MENOPAUSE. For relieving the nervous symptoms and physical distress so often observed during the climacteric, BROMO-MANGAN can be relied on in every particular."

A circular says that:

"In the treatment of Chorea, BROMO-MANGAN gives very prompt relief from nervous excitability, and . . . rapidly restores the patient to health."

"In neuroses, complicating blood impoverishment, BROMO-MANGAN has its most important field of indication."

This is not supported by evidence. A circular purporting to be an abstract of a lecture by von Grimm, delivered at the New York Post Graduate Medical School and Hospital is at the most an unsupported statement of a personal opinion:

"Bromo-mangan. This specific composition of an organic Bromine with its quieting, pain-alleviating effect, in combination with organic Iron and Manganese, the one creation of modern science, which has beyond all dispute made good its claim to possess the power of increasing metabolism of the blood creating cells—appealed to me."

The Council voted to omit Bromo-Mangan from future editions of New and Nonofficial Remedies for conflict with Rule 6 (unwarranted therapeutic claims) and Rule 10 (unscientific composition).

Elixir Buchu, Juniper and Acetate Potassium Omitted from N. N. R.

Elixir Buchu, Juniper and Acetate Potassium (Pitman-Moore Co., Indianapolis) was submitted and accepted for N. N. R. in 1908, before the adoption of the present Rule 10.

Buchu and juniper were once largely used. Each contains volatile oil which is a renal irritant. While these oils may be useful in some cases, there is no clear indication for their use in combination with potassium acetate. If a saline diuretic is needed, there is no obvious occasion to give an irritant diuretic. It may be argued (and probably with justice) that there is not enough oil present in this elixir to act as a renal irritant. In that case, however, the amount present is likewise insufficient to act as an efficient urinary antiseptic; and its presence may lead the physician to withhold an efficient urinary antiseptic under the belief that he is using one. (There are better urinary antiseptics than the oils of buchu and juniper.)

Holding that mixtures of this sort are never distinctly indicated, and are sometimes distinctly harmful, the Council voted that Elixir Buchu, Juniper and Acetate Potassium be deleted from New and Nonofficial Remedies for conflict with Rule 10.

Tyree's Elixir of Buchu and Hyoscyamus Compound

Each dessertspoonful of this preparation is said to represent

"Buchu Leaves ..... 3½ grains
Uva Ursi ..... 1⅛ grains
Pareira Brava ..... 1⅛ grains
Hyoscyamus ..... 1½ grains
Hops ..... 1½ grains
Acetate Potash ..... 7½ grains
Spirits Nitre ..... 5 grains
Alcohol .....5 per cent. (by volume)"

The manufacturer, J. S. Tyree, Washington, D. C., offers this formula to the medical profession with the following claim:

"Approximate composition made [sic] by quantitative and qualitative analysis of the finished product."

It is also claimed that

"An even greater advantage of Tyree's Buchu and Hyoscyamus Compound over other drugs, lies in the fact that every constituent of the former is required to conform to a fixed standard of active principle strength; hence the results derivable from it are absolutely uniform."

These pretentious claims of scientific accuracy look rather absurd to chemists. Many of the substances present in buchu, hops, hyoscyamus, uva ursi and pareira brava are also present in other drugs; hence it would never occur to a pharmaceutical chemist to try to ascertain the composition of such a mixture as Tyree's Elixir by "quantitative and qualitative analysis of the finished product," much less to determine the "active principle strength" or each ingredient, for no methods are known by which this can be done.

It is claimed that, because of the care exercised in making Tyree's Elixir

". . . the results derivable from it are absolutely uniform."

A moment's reflection, however, must compel any physician to attribute this statement, on the most charitable construction, to sheer ignorance. Of course, even a definite chemical principle, such as quinin, does not exert uniform clinical action, for clinical conditions vary, and accordingly the patient may or may not be cured. It is simply preposterous to claim that the clinical results obtained from such substances as hops, pareira brava, buchu and uva ursi are absolutely uniform.

A peculiarly vicious claim is that the elixir renders the mucous surfaces of the genito-urinary tract "hostile to the multiplication of the gonococci." Since infection with the gonococcus produces the direst results, any claim which means in plain English that the remedy assists in producing a cure or in preventing infection with that organism cannot be condemned too strongly. Uva ursi, to be sure, has some slight antiseptic action but it is devoid of any curative

action in gonorrhea and the minute amounts that are present in the Tyree elixir are of no more protective value against gonorrheal infection than a grain of hexamethylenamin would be.

It is further claimed that the elixir is a "specific" for "Inflammation of the Bladder, Bright's Disease, Renal Colic, Suppurative Nephritis, Acute Cystitis, Urethritis, Catarrh of the Bladder [it would be interesting to know what distinction the manufacturer draws between 'Inflammation of the Bladder,' 'Cystitis' and 'Catarrh of the Bladder'], Acidemia, Edema, Vesical Catarrh of Old Age, Lithemia" and that ascites and anasarca "can be reduced greatly to the satisfaction of the patient, and honor of the physician" by using a mixture of Tyree's Elixir and infusion of digitalis. Such claims as these do not merit serious discussion, for they carry their own refutation.

It is recommended that Tyree's Elixir of Buchu and Hyoscyamus Compound be held in conflict with Rules 5, 6 and 10 and that publication of this report be authorized.

Syrup Cannabis Compound Omitted from N. N. R.

Syrup Cannabis Compound (Pitman-Moore Company, Indianapolis) is said to contain, or to represent, in each fluidounce, 7½ grains cannabis indica, ⅓ grain heroin hydrochlorid, 4 minims chloroform, 7½ grains lobelia, and ⅛ grain antimony and potassium tartrate with aromatics, syrup and 10 per cent. alcohol.

It was submitted to the Council and accepted for inclusion in N. N. R. in 1908—that is, previous to the adoption of the present Rule 10.

It has become increasingly apparent that cannabis indica is therapeutically useless. We know little about its chemistry, but its active therapeutic principles are apparently insoluble in water.

It is impossible to determine just how much of the activity of the compound syrup of cannabis depends on the heroin and how much on the cannabis. It is obviously in conflict with Rule 10. In view of this the Council voted that it be omitted from future editions of New and Nonofficial Remedies.

Calol Liquid Petrolatum Omitted from N. N. R.

The Standard Oil Company of California informed the Council that its output of liquid petrolatum had been disposed of and that Calol Liquid Petrolatum, Heavy, was no longer being offered for sale. Accordingly the Council directed that the description of Calol Liquid Petrolatum, Heavy, be omitted from N. N. R.

Chinaphenin Omitted from N. N. R.

The Council was informed by the Bayer Company, Inc., the American agents for Chinaphenin, that this product has been

practically withdrawn from the market. Accordingly the Council voted that the description of this product be omitted from future editions of New and Nonofficial Remedies.

Colchi-Methyl Capsules Omitted from N. N. R.

Colchi-Methyl Capsules (H. K. Wampole & Company) are said to contain, in each, colchicin 0.00025 gm., phenyl salicylate (salol) 0.13 gm. and methyl salicylate 0.2 c.c.

This preparation was admitted to New and Nonofficial Remedies before the rules of the Council were revised to require that the names of pharmaceutical mixtures admitted to N. N. R. must indicate their potent ingredients, and before the Council had adopted the present Rule 10:

"No article will be admitted which, because of its unscientific composition, is useless or inimical to the best interests of the public or the medical profession."

The name "Colchi-Methyl Capsules" does not sufficiently indicate the constituents. Further, it is well known that different cases require different doses of salicylate. Hence the combination of salicylates with so dangerous a drug as colchicine is irrational and cannot be recognized under the present rules of the Council.

The Council voted that Colchi-Methyl Capsules be omitted from future editions of N. N. R.

Emulsio Minerolein and Emulsio Phen-Oleum

The T. R. D. Barse Company, New York, markets the following preparations of liquid petrolatum: Emulsio Minerolein, Plain, containing 240 minims of liquid petrolatum in each fluidounce; Emulsio Minerolein with Bismuth, containing 120 minims liquid petrolatum and 60 grains bismuth subcarbonate in each fluidounce; Emulsio Minerolein with Castor Oil, containing 120 minims liquid petrolatum and 120 minims castor oil in each fluidounce; Emulsio Minerolein with Bismuth and Castor Oil, containing 72 minims of liquid petrolatum, 24 minims castor oil and 60 grains bismuth subcarbonate in each fluidounce; Emulsio Minerolein with Salol and Castor Oil containing 96 minims liquid petrolatum, 24 minims castor oil and 20 grains salol in each fluidounce and Emulsio Phen-Oleum with Phenolphthalein containing 160 minims liquid petrolatum and 6 grains phenolphthalein in each fluidounce.

The Council holds that in the case of pharmaceutical mixtures of well-known medicaments, the names should be so framed as to indicate the potent ingredients. The term "Minerolein" is regarded as insufficiently descriptive of the well-known and official liquid petrolatum and the term "Phen-Oleum" as nondescriptive of a mixture of phenolphthalein and liquid petrolatum (the term "Phen-Oleum" has also been applied to a phenol disinfectant).

The Council held the several preparations listed above ineligible either for New and Nonofficial Remedies or the appendix to New and Nonofficial Remedies.

Glutol-Schleich Omitted from N. N. R.

Glutol-Schleich is a compound of gelatin and formaldehyd. It is manufactured by the Chemische Fabrik auf Aktien, vorm. E. Schering, Berlin, and sold in the United States by Schering and Glatz, New York. It is described in New and Nonofficial Remedies, 1915, the following statement of "Actions and Uses" being given:

"It is claimed that, while in itself non-antiseptic, non-irritant and non-toxic, glutol becomes antiseptic and bactericidal on contact with living cells, in consequence of the elimination of nascent formaldehyde, which is split off very slowly but steadily.

"Glutol is said to be useful as an odorless, non-irritant, non-poisonous aseptic dressing, having sustained antiseptic action for wounds, ulcers, burns, etc. The greater part of the formaldehyde, however, is held so firmly that it is of slight efficiency."

A referee reported to the Council that Glutol-Schleich apparently had failed to justify expectations and that it had practically gone out of use. He reported that the experiments of T. Sollmann (THE JOURNAL, Sept. 5, 1908, p. 824; Reports Council Pharm. and Chem., 1908) had shown that the specific liberation of formaldehyd from Glutol by the action of living cells is somewhat doubtful. Sollmann found that the quantity of formaldehyd liberated from Glutol by pancreatic digestion (which is analogous to digestion by living cells) is not sufficient to check putrefaction markedly; that Glutol is inferior as a preservative to nearly all the other substances which were tried, and that its efficiency on the blood was also poor.

The conclusions of Sollmann were submitted for comment to the American agents, who admitted that they had no recent authoritative pharmacologic or clinical evidence to contradict them. The Council therefore voted to omit Glutol-Schleich from future editions of New and Nonofficial Remedies.

Pill Glycero-Lecithin

Pill Glycero-Lecithin (Westerfield Pharmacal Co., Dayton, Ohio) is said to contain, in each:

"Lime Glycerophosphate	1 gr.
Iron Glycerophosphate	1-2 gr.
Quinine Glycerophosphate	1-8 gr.
Strychnine Glycerophosphate	1-240 gr.
Lecithin	1-4 gr."

The following therapeutic claims are made:

"The glycerophosphates are valuable in the treatment of functional disturbances of the nervous system and in various organic disorder,

due to faulty metabolism. They supply phosphorous to the system in the form in which it must be converted before it is assimilated. It is therefore the physiological nerve food. The Glycerophosphates of quinine and strychnine supply the tonic properties in this formula.

"Lecithin is the phosphorous holding molecule of the central nervous system. It increases weight and is highly recommended in run-down nervous cases and nervous debility resulting from mental strain.

"DOSE—1 to 2 tablets four times a day."

The Council holds the therapeutic claims unwarranted for the following reasons: A preponderance of evidence indicates that the human organism can synthesize its phosphorus supply from inorganic phosphorus compounds; if organic phosphorus is desired, it is more advantageously given, and in more efficient amounts, in the form of natural lecithins found in milk and egg yolk. Moreover, the name is nondescriptive and misleading; it does not indicate the presence of calcium, quinin, strychnin, glycerophosphates; instead it emphasizes a therapeutically unimportant ingredient—lecithin. Further, the Council holds the combination of calcium, quinin and strychnin, and glycerophosphates and lecithin to be irrational and conducive to uncritical medication. The Council therefore declared Pill Glycero-Lecithin inadmissible to N. N. R.

The report was sent to the Westerfield Pharmacal Company in accordance with the Council's regular procedure. The manufacturer having offered no evidence permitting a revision of the report, the Council authorized its publication.

Hydroleine

Hydroleine (Charles N. Crittenton Company, New York) is a cod liver oil emulsion said to contain 45 per cent. of cod liver oil, a trace of salicylic acid and 18½ grains of "Pancreatin, Etc.," per ounce. The advertising claims are based largely on the theory that cod liver oil is "that particular fat which dietetic experience and physiological chemistry have proved to be most digestible." As a matter of fact, while the superior digestibility of cod liver oil over other oils has often been asserted, neither "dietetic experience" nor "physiological chemistry" have "proved" this by definite observations. The Crittenton Company claims that it is more readily split than other oils. This is probably not true, easy emulsification of the raw oil being often confounded with easy splitting. This latter claim, however, is offered in justification of the name "Hydroleine," which the Crittenton Company interprets as "hydrated oil." A circular wrapped around the bottle contains the assertion that "Cod Liver Oil has long been held in high esteem by the medical profession for the treatment of a large number of serious diseases." This recommendation is likely to lead the public to place undue reliance on Hydroleine in the grave conditions mentioned.

The preparation is in conflict with the rules of the Council inasmuch as its name does not indicate its composition,

unwarranted therapeutic claims are made for it, and the exploitation is likely to give the public unwarranted confidence in its value. The Council therefore held Hydroleine ineligible for New and Nonofficial Remedies.

Isatophan and Paratophan Omitted from N. N. R.

Schering and Glatz, who represent the manufacturers of Isatophan and Paratophan, have informed the Council that Isatophan and Paratophan were merely experimental products which have been superseded by Novatophan. The Council therefore directed that Isatophan and Paratophan be omitted from New and Nonofficial Remedies.

Koyol

Koyol (The Koyol Co., New York) is said to be composed of liquid petrolatum 35 per cent., petrolatum 22 per cent., lanolin 25 per cent., egg albumin 12 per cent., cantharides 3 per cent., sulphur 2 per cent., with perfume extract 1 per cent.

The claim that Koyol, "The Scientific Preservative for the Hair," "is a means for overcoming ailments caused by malnutrition, such as splitting and knotting of hair, falling out before full growth is attained" and similar claims made in the advertising circular are unwarranted and irrational.

The Council refused recognition to Koyol because unwarranted therapeutic claims were made for it (Rule 6), because its complex composition rendered it unscientific (Rule 10) and because the name of the pharmaceutical mixture was not descriptive of its composition (Rule 8).

Med-O-Lin

Med-O-Lin (Waverly Oil Works Company, Pittsburgh, Pa.) is a light liquid petrolatum, odorless, not quite tasteless and somewhat fluorescent. It is advertised so as to create the impression that it is a distinct product. The advertising lays stress on the claim that the product is purified without the use of chemicals. The Council advised the company that the product could be made eligible for N. N. R. if it were made colorless and non-fluorescent in compliance with the description of heavy liquid petrolatum in THE JOURNAL for May 30, 1914, if the advertising matter were suitably revised and if on the labels and in the advertisements and circulars the words "Liquid Petrolatum" were used as a part of the brand designation and given equal prominence with the term "Med-O-Lin." The Waverly Oil Works Company expressed willingness to modify the name and the advertising so as to comply with the requirements of the Council if the product were accepted, but was unable to make the product itself

absolutely colorless and non-fluorescent. The Council held that it would be a step backward to accept a preparation which was not colorless and non-fluorescent and therefore voted not to accept Med-O-Lin.

Methyl-Santal Omitted from N. N. R.

Methyl-Santal (H. K. Mulford Company) is said to contain in each capsule methylene blue 0.06 gm., oleoresin of copaiba 0.1 c.c., oleoresin of cubebs, 0.025 c.c., oil of sandalwood, 0.09 c.c. of cinnamon, 0.013 c.c. and oil of nutmeg, 0.005 c.c.

This preparation was admitted to New and Nonofficial Remedies before the rules of the Council were revised to require that the names of pharmaceutical mixtures admitted to N. N. R. must indicate their potent ingredients, and before the Council had adopted the present Rule 10:

"No article will be admitted which, because of its unscientific composition, is useless or inimical to the best interests of the public or the medical profession."

The name "Methyl-Santal" is not sufficiently indicative of the ingredients. Moreover, the mixture contains at least four ingredients supposed to act as urinary antiseptics, a combination in favor of which there is no satisfactory evidence.

The Council voted that Methyl-Santal be omitted from future editions of N. N. R.

Neurocaine Omitted from N. N. R.

Neurocaine (Schieffelin & Co.) is cocain hydrochlorid compressed into "billets" for dental practice.

This preparation was admitted to New and Nonofficial Remedies before the rules of the Council were revised to require that the names of pharmaceutical mixtures admitted to N. N. R. must indicate their potent ingredients.

Under the present ruling Neurocaine is ineligible for continuance in New and Nonofficial Remedies.

The manufacturers refused to comply with a suggestion that, by adopting a properly descriptive name, they make possible the continuance of this preparation in N. N. R.

The Council voted that Neurocaine be omitted from future editions of N. N. R.

Oxyntin Omitted from N. N. R.

Protein-hydrochloric acid combinations of the type of Oxyntin, as the experiments of Long have shown (*Jour. Amer. Chem. Soc.*, May, 1915, p. 1333), are scarcely able to digest their own protein when treated with pepsin, much less to aid in the digestion of any additional weight of protein. The excess of protein in the combination is such as greatly to lower the activating value of the acid.

The actual amount of acid which may be administered through such compounds is small. With a dose of from 5 to 15 grains (from 0.33 gm. to 1 gm.) of Oxyntin as recommended, the hydrochloric acid dosage is from 17 to 50 mg. Such amounts, being insignificant in comparison with the amount of hydrochloric acid normally secreted, are altogether insufficient to meet the needs of digestion in cases of failure of the normal secretion.

The dissociation, when mixed with water, of bodies of the type of Oxyntin is comparatively slight, and so, consequently, is the degree of actual acidity which may be thus obtained. The hydrogen ion concentration, which is doubtless the most important factor in the several functions of the acid, is low, from the nature of the compound.

Therefore, the Council voted that Oxyntin be omitted from future editions of New and Nonofficial Remedies.

The preceding report having been sent to the manufacturers, they replied that they naturally have no contentious attitude as to therapeutic value or particular usefulness of Oxyntin, but that their attitude is primarily based on what the product is and the need of betterment in the means of clinical administration of hydrochloric acid. Fairchild Brothers and Foster further state that in future discussions of Oxyntin they would take occasion to refer to the Council's findings.

Piperazine-Schering Omitted from N. N. R.

The Council was informed by Schering and Glatz that they no longer sell Piperazine-Schering. Accordingly the Council voted that the name of Schering and Glatz be omitted from the names of the selling agents for Piperazine.

Ricinol-Grape Tape-Worm Remedy and Baby Taeniafuge-Grape

Ricinol-Grape Tape-Worm Remedy, sold by the Grape Capsule Co., New York, consists of two kinds of capsules, one said to contain castor oil and the other said to contain oleoresin of male-fern, fluid extract of kamala and castor oil.

Baby Taeniafuge-Grape, a tape-worm remedy for children, consists of capsules said to contain oleoresin of male-fern, extract of cascara sagrada and castor oil, the latter being referred to as "Ricinol Grape" the firm's trade-marked name for castor oil capsules.

The Council refused recognition to these preparations because they were marketed in a way to encourage their use by the public to its detriment (Rule 4), because the names were therapeutically suggestive and not descriptive of composition as required by the Council (Rule 8) and because the administration of male-fern and castor oil is not safe as a routine practice (Rule 10).

Tubo-Arg

Tubo-Arg (Tubo Pharmacal Company, Duluth, Minn.) is said to be a tragacanth jelly containing 0.2 per cent. albargin. This jelly is put up in collapsible tubes that permit its direct injection into the anterior urethra; it is advertised as an efficient remedy for the treatment of gonorrheal urethritis.

The injection of a jelly containing but 0.2 per cent. of albargin, which contains 13 to 15 per cent. silver (and this is advised in the circular as the sole treatment), can have little germicidal action on the gonococcus. Even if Tubo-Arg were possessed of material germicidal action, the recommended treatment would be inefficient, because the gonococcus buries itself within the tissue cells where, without dilatation, it cannot be reached by simple injections of any sort. In addition, it is not to be expected that the proposed method of injection will affect the entire urethra.

While the circular enclosed with the trade package is addressed to the physician, it is of a character which will appeal to the public. Thus it is likely to induce sufferers from the disease to attempt self-treatment with this inefficient preparation.

Tubo-Arg is sold under unwarranted therapeutic claims and under a name that is nondescriptive of its composition. It is exploited in a way that is likely to lead the public to attempt self treatment of gonorrhea with this worthless preparation to their own harm and to the public danger.

Tubo-Arg is inadmissible to New and Nonofficial Remedies because it is in conflict with Rules 4, 6, 8 and 10.

Ulax Salt

Ulax Salt is a saline laxative of the Sal Hepatica type (THE JOURNAL, Feb. 7, 1914, p. 472) which the medical profession is asked to introduce to the public. The F. H. Strong Company, which exploits it, offers the following noninforming statement of composition:

"A 'straight' effervescent saline laxative composed of Sodium Sulphate, Sodium Phosphate, and a peculiarly 'clean'-tasting effervescent laxative base."

The label on a package "Price 25 cents" contains the following recommendation:

"Of special service as a brisk laxative in Constipation, Inactive Liver, Dyspepsia, Chronic Headache, Auto-intoxication, Rheumatic and Gouty Disorders, and after Alcoholic Excesses."

It is said to be

". . . perfectly safe as a laxative for Diabetic, Rheumatic, Gouty or Dyspeptic patients. . . ."

Ulax Salt is not accepted for New and Nonofficial Remedies because its composition is essentially secret and because unwarranted recommendations are made for it; moreover, its suggestive name and its method of exploitation tend to encourage the excessive and harmful use of saline cathartics by the public.

Uranoblen and Caviblen

Uranoblen, a silver compound of Uranin (sodium fluorescein) eosin, forms the basis of bougies, "Caviblen Hohlstäbchen," to be used in the treatment of gonorrhea by what is referred to by A. Grimme, the American agent, as "Prof. Bruck's Caviblen Therapy of Gonorrhea." Objection having been made to the term "Caviblen Hohlstäbchen" as not indicating the active constituent of these bougies, the agent proposed instead the name "Uranoblen in Caviblen Bougies." The Council held the terms "Uranoblen" and "Caviblen" to be therapeutically suggestive and in view of the very great danger from the self treatment of gonorrhea or even the uncritical treatment of the disease by the medical profession, voted that Uranoblen and Uranoblen in Caviblen Bougies be refused recognition for conflict with Rule 8.

Curative Vaccine, Bruschettini

Curative Vaccine, Bruschettini, manufactured by A. Bruschettini, Genoa, Italy, is claimed to have the properties "of acting directly on the tubercular bacillus, bringing directly into the field and determining a hyperproduction of antibacillar and antitoxic substances." The use of the preparation is said to be indicated in "all forms of tuberculosis."

A referee reported to the Council that he had examined the available information and believed that the use of this product had no satisfactory experimental basis. The method of preparation appears to be based more on theoretical considerations than on experimental basis.

On the recommendation of the Committee on Serums and Vaccines the Council voted that Curative Vaccine, Bruschettini, be not accepted because (1) the method used for the production of the vaccine was not satisfactorily stated; (2) the theory on which its use is based has not been satisfactorily confirmed, and (3) the value of the product is not upheld by satisfactory clinical evidence.

The Council's findings, in accordance with its procedure, were sent to the manufacturer for comment. His reply was considered by a new referee who found that the matter presented did not warrant a revision of the Council's conclusions. Accordingly the Council directed publication of its findings.

Stearns' Wine

Frederick Stearns & Co. market a preparation known as "Stearns' Wine," "Stearns' Wine of Cod Liver Ext. with Peptonate of Iron," and as "Vinum Ext. Morrhuae, Stearns." The constituents are said to be "concentrated extract of fresh cod livers," "Peptonate of Iron" and a "fine quality of prime Sherry Wine" containing 18 per cent. of alcohol.

This preparation was at one time marketed through the medical profession, but is now advertised direct to the public in typical "patent medicine" style. The label on a recently purchased bottle of Stearns' Wine contains the following statements:

"STEARNS WINE is an ideal tonic for elderly people, for weak, pale and delicate children and convalescents.

"STEARNS WINE has for many years been successfully prescribed in the treatment of general or nervous exhaustion, anemia, malnutrition, loss of appetite, loss of sleep, faulty circulation and impoverished blood supply."

The scope of the recommendations for the preparation is further indicated in a booklet accompanying the bottle, which begins:

STEARNS' WINE, What It Is and Why It Is Good for You."

The conclusion is:

"STEARNS' WINE is a safe medicine for the young, middle-aged and old. It is a safeguard to the family health."

It is not necessary to discuss either these all-embracing claims as to the therapeutic efficacy of the mixture or the fallacies presented in favor of cod-liver extract and peptonate of iron. The Council reaffirms the opinion that whatever therapeutic value cod liver may have resides chiefly, if not entirely, in its fatty constituents (THE JOURNAL, Oct. 9, 1909; Reports Council Pharm. and Chem., 1909, p. 115). A confirmation of this opinion has recently been furnished by the investigations of Prof. J. P. Street (THE JOURNAL A. M. A., Feb. 20, 1915, p. 638) of several cod liver cordials, one of which (Vinol) like Stearns' Wine, is described as a wine of cod liver extract with peptonate of iron.

Stearns' Wine is essentially an alcoholic stimulant. It is not "a safe medicine for the young, middle-aged and old." The unwarranted therapeutic claims and the recommendations for its indiscriminate use bring it into conflict with Rules 4 and 6. The Council voted that Stearns' Wine be held ineligible for inclusion in N. N. R.

INDEX OF PROPRIETARIES, MANUFACTURERS AND AGENTS

PAGE

Abbott Laboratories.
Neuro-Lecithin-Abbott 123
Adrenalin and Cocain Ointment-M. E. S. Co. Omitted from N. N. R..... 162
Agurin Tablets. Omitted from N. N. R..... 162
Alfatone 62
Alypin Tablets, 3⅓, 1⅛ and ¾ grain. Omitted from N. N. R..... 162
American Malt Extract Co.
Williams' Syrup of Malt..... 155
Analutos and Analutos Tablets..... 135
Anglo-American Pharmaceutical Co.
Colchi-Sal 136
Anistamina 162
Antipyrin Salicylate-Farbwerke. Omitted from N. N. R..... 164
Armour & Co.
Duodenin, Armour 151
Lecithol. Omitted from N. N. R..... 123

Baby Taeniafuge-Grape 174
Ballard, J. F.
Tri-Iodides, Three Chlorides and Maizo-Lithium..... 9
Barse, T. R. D., Co.
Emulsio Minerolein and Emulsio Phenoleum..... 169
Bauer Chemical Co.
Formamint 64
Bayer Co., Inc.
Agurin Tablets, Alypin Tablets, Hedonal Tablets, Iodothyrine Tablets and Tannigen Tablets. Omitted from N. N. R..... 162
Chinaphenin. Omitted from N. N. R..... 168
Betanaphthol Benzoate-Heyden 164
Betol-Heyden 164
Bischoff, C., & Co.
Eupyrine, Fortoin, Quinine Lygosinate and Sodium Lygosinate. Omitted from N. N. R..... 164
Hydragogin 154
Bischoff, E., & Co.
Digitalysatum 93
Hydropsin 94
Blaud Capsules, Frosst's..... 164
Bornyval 164
Brobor 164
Bromo-Mangan 165
Bruschettini, A.
Curative Vaccine, Bruschettini..... 176
Buchu and Hyoscyamus Compound, Tyree's Elixir of..... 167
Buchu, Juniper and Acetate Potassium Elixir. Omitted from N. N. R..... 166

PAGE

Budwell Pharmacal Co.
Budwell's Emulsion of Cod Liver Oil, Nos. 1 and 2 135
Burnham Soluble Iodine Company.
Burnham's Soluble Iodine 50

Calcreose 147
Calol Liquid Petrolatum. Omitted from N. N. R. 168
Cannabis Compound, Syrup. Omitted from N. N. R. 168
Carnrick, G. W., Co.
Secretogen 46, 97
Caviblen 176
Chatelain, J. L.
Filudine 156
Globeol 157
Jubol 152
Urodonal 153
Chemische Fabrik auf Aktien, vorm. E. Schering.
Glutol-Schleich 170
Chemische Fabrik Helfenberg, A. G.
Bromo-Mangan 165
Chemotherapy and Tumors 28
Chinaphenin. Omitted from N. N. R. 168
Chionia 24, 26
Cocain and Adrenalin Ointment-M. E. S. Co. 162
Cod Liver, Extract of, Wampole's Perfected and Tasteless Preparation of 140
Cod Liver Oil Compound, Waterbury's (Waterbury's Compound) .. 138
Colchi-Methyl Capsules. Omitted from N. N. R. 169
Colchi-Sal 136
Colloidal Treatment of Tumors 28
Crittenton, Charles N., Co.
Hydroleine 171
Cuprase 29
Curative Vaccine, Bruschettini 176

Delays in Passing on Products 119
Digitalis Preparations, Proprietary 89
Digitalysatum 93
Dolomol Chrysarobin 5 per cent., Dolomol Europhen 10 per cent., Dolomol Naphthol 5 per cent., Dolomol Pyrogallic Acid 5 per cent., Dolomol Salol 10 per cent., Dolomol Tar 10 per cent., and Dolomol Thymol 2 per cent. Omitted from N. N. R. 162
Duodenin, Armour 114, 151

Electro-Selenium 29
Elixir Buchu, Juniper and Acetate Potassium. Omitted from N. N. R. 166
Elixir of Buchu and Hyoscyamus Compound, Tyree's 167
Elixir Iodo-Bromide of Calcium Compound, "Without Mercury" and "With Mercury" 160
Elixir Lactopeptine 79
Elixir Secretogen 112
Emulsio Minerolein 169
Emulsio Phen-Oleum 169
Eosin-Selenium 32

PAGE
Episan 164
Euphorin. Omitted from N. N. R..... 164
Eupyrine. Omitted from N. N. R..... 164
Fabrik von Heyden.
Euphorin. Omitted from N. N. R..... 164
Fa. Episan Berensdorf.
Brobor (Episan) 164
Fairchild Bros. & Foster.
Glycerole of Lecithin, Lecibrin and Lecithin Solution. Omitted from N. N. R..... 123
Oxyntin. Omitted from N. N. R..... 174
Farbwerke Hoechst Co.
Antipyrin Salicylate-Farbwerke and Gujasanol. Omitted from N. N. R..... 164
Filudine 156
Formamint 64
Fortoin. Omitted from N. N. R..... 164
Fortossan 131
Fougera, E., & Co.
Colchi-Sal 136
Franco-American Ferment Co.
Lactobacilline Products. Omitted from N. N. R..... 143
Frederick, Purdue Co.
Gray's Glycerine Tonic Compound..... 56
Friedländer Bacterin-Mulford 164
Frosst, C. E., & Co.
Frosst's Blaud Capsules and Frosst's Blaud, Arsenic and Strychnine Capsules 164
Gaynor-Bagstad Co.
Brobor (Episan) 164
G. G. Chemical Co., Inc.
G. G. Phenoleum Disinfectant..... 131
Globeol 157
Glutol-Schleich. Omitted from N. N. R..... 170
Glycero-Lecithin Pill 170
Glycerole of Lecithin. Omitted from N. N. R..... 123
Grape Capsule Co.
Ricinol-Grape Tape-Worm Remedy and Baby Taeniafuge-Grape... 174
Gray's Glycerine Tonic..... 56
Grimme, A.
Uranoblen and Caviblen..... 176
Guaiacodeine. Omitted from N. N. R..... 164
Gujasanol. Omitted from N. N. R..... 164
Hedonal Tablets, 8 Grain. Omitted from N. N. R..... 162
Henry Pharmacal Co.
Three Chlorides, Tri-Iodides and Maizo-Lithium..... 9
Hexa-Co-Sal-In Co.
Hexa-Co-Sal-In 159
Hoffmann-LaRoche Chemical Works.
Pantopon Roche (Pantopium Hydrochloricum). Accepted for N. N. R..... 126
Hydragogin 154
Hydroleine 171
Hydropsin 94

PAGE

Intravenin Products Co.
Intravenin P-H 120
Intravenous Products Co.
Venarsen 52
Venodine 145
Iodex 144
Iod-Izd-Oil (Miller's) 76
Iodo-Bromide of Calcium Compound, Elixir "With Mercury" and "Without Mercury" 160
Iodothyrine Tablets, 5 Grain. Omitted from N. N. R. 162
Iodum-Miller Co.
Iodum-Miller and Iod-Izd-Oil (Miller's) 76
Isatophan. Omitted from N. N. R. 172

Jubol 152

Klipstein, A., & Co.
Phytin and Fortossan 131
Koyol Co.
Koyol 172

Lactobacilline. Omitted from N. N. R. 143
Lactopeptine 79
Lecibrin. Omitted from N. N. R. 123
Lecithin Preparations. Omitted from N. N. R. 122
Lecithin Solution. Omitted from N. N. R. 123
Lecithol. Omitted from N. N. R. 123
Lilly, Eli, & Co.
Rheumalgine 148
Liquid Petrolatum, Proprietary Names for 127

Maizo-Lithium 9, 14
Maltbie Chemical Co.
Calcreose 147
Malt, Williams' Syrup of 155
Manhattan Eye Salve Co.
Cocain and Adrenalin Ointment-M. E. S. Co. 162
Marchesini, Dr. Carlo.
Anistamina 162
Marcy Co.
Veracolate 141
Med-O-Lin 172
Melachol 150
Mellier Drug Co.
Tongaline and Ponca Compound 59
Menley & James, Ltd.
Iodex 144
Methyl-Santal. Omitted from N. N. R. 173
Mulford, H. K., Co.
Friedländer Bacterin-Mulford, and Predigested Liquid Food-Mulford. Omitted from N. N. R. 164
Methyl-Santal. Omitted from N. N. R. 173

Neurilla 20
Neurocaine. Omitted from N. N. R. 173
Neuro-Lecithin-Abbott. Omitted from N. N. R. 123

PAGE

New York Pharmacal Association.
Lactopeptine and Elixir Lactopeptine 79
New York Quinine & Chemical Works.
Guaiacodeine. Omitted from N. N. R. 164
New York Salesthyl Corporation.
Salesthyl and Sal-Hyl 134
Norwich Pharmacal Co.
Alfatone 62

Od Chemical Company.
Sanmetto 17
Olivetti, M.
Anistamina 162
Oxyntin 174

Pantopon Roche (Pantopium Hydrochloricum). Admitted to N. N. R. 126
Paratophan. Omitted from N. N. R. 172
Peacock Chemical Company.
Peacock's Bromides and Chionia 24
Petrolatum, Calol Liquid. Omitted from N. N. R. 168
Petrolatum, Liquid, Proprietary Names for 127
Phytin 131
Pill Glycero-Lecithin 170
Piperazine-Schering. Omitted from N. N. R. 174
Pitman-Moore Co.
Elixir Buchu, Juniper and Potassium Acetate. Omitted from N. N. R. 166
Syrup Cannabis Compound. Omitted from N. N. R. 168
Plesner, Paul, Co.
Taurocol 143
Ponca Compound 58, 61
Predigested Liquid Food-Mulford. Omitted from N. N. R. 164
Protonuclein and Protonuclein Beta 90
Pulvola Chemical Co.
Dolomol Pyrogallic Acid, 5 Per Cent.; Dolomol Chrysarobin, 5 Per Cent.; Dolomol Europhen, 10 Per Cent.; Dolomol Naphthol, 5 Per Cent.; Dolomol Salol, 10 Per Cent.; Dolomol Tar, 10 Per Cent., and Dolomol Thymol, 2 Per Cent. 162
Purdue Frederick Co.
Gray's Glycerine Tonic 56

Quinine Lygosinate. Omitted from N. N. R. 164

Radio-Active Water Co.
Radelium and Radelium Generator 128
Radium Chemical Co.
Standard Radium Solution for Intravenous Use 147
Reed & Carnrick.
Protonuclein and Protonuclein Beta 90
Reinschild Chemical Co.
Bromo-Mangan 165
Rheumalgine 148
Rheumatic Bacterin (Mixed) No. 47, Swan's 160
Ricinol-Grape Tape-Worm Remedy 174

Riedel & Co. PAGE
Bornyval. Omitted from N. N. R. 164
Xerase Capsules. Omitted from N. N. R. 162
Royal Pharmaceutical Works.
Analutos and Analutos Tablets 135

Salesthyl 134
Sal-Hyl 134
Sanmetto 17
Schering & Glatz.
Glutol-Schleich. Omitted from N. N. R. 170
Isatophan and Paratophan. Omitted from N. N. R. 172
Oxyntin. Omitted from N. N. R. 174
Schieffelin & Co.
Neurocaine. Omitted from N. N. R. 173
Secretin, Has It a Therapeutic Value? 99
Secretin Preparations, So-Called 96
Secretogen (Elixir and Tablets) 46, 97, 112
Selenium Compounds 28
Seng 129
Society of Chemical Industry.
Phytin and Fortossan 131
Sodium Lygosinate. Omitted from N. N. R. 164
Standard Oil Co.
Calol Liquid Petrolatum. Omitted from N. N. R. 168
Standard Radium Solution for Intravenous Use 147
Stearns, Frederick & Co.
Stearns' Wine 177
Strong, F. H., Co.
Ulax Salt 175
Sulpho-Selene 29
Sultan Drug Co.
Seng 131
Swan-Myers Co.
Swan's Rheumatic Bacterin (Mixed) No. 47 160
Syrup Cannabis Compound. Omitted from N. N. R. 168

Tannigen Tablets. Omitted from N. N. R. 162
Taurocol Compound Tablets 143
Three Chlorides (Henry) 9, 12
Tilden Co.
Elixir Iodo-Bromide of Calcium Compound, "Without Mercury" and "With Mercury" 160
Tongaline, Tongaline and Lithia Tablets, Tongaline and Quinine Tablets, and Tongaline Tablets 58
Tri-Iodides (Henry) 9
Tubo Pharmacal Co.
Tubo-Arg 175
Tyree, J. S.
Tyree's Elixir of Buchu and Hyoscyamus Compound 167

Ulax Salt 175
Uranoblen 176
Uricsol Chemical Co.
Uricsol 149
Urodonal 153

PAGE
Venarsen 52
Venodine 145
Veracolate (plain), Veracolate with Pancreatin and Pepsin, and Veracolate with Iron, Quinine and Strychnine 141
Virol, Ltd.
Virol 132

Wallau, Geo. J., Inc.
Filudine 156
Globeol 157
Jubol 152
Urodonal 153
Wampole, Henry K., & Co., Inc.
Colchi-Methyl Capsules 169
Wampole's Perfected and Tasteless Preparation of an Extract of Cod Liver 140
Waterbury Chemical Co.
Waterbury's Compound 138
Waverly Oil Works Co.
Med-O-Lin 172
Westerfield Pharmacal Co.
Pill, Glycero-Lecithin 170
Williams' Syrup of Malt 155
Wulfing, A., Co.
Formamint 64

Xerase Capsules 162